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*answer search*  
 (FILE 'STNGUIDE' ENTERED AT 09:56:52 ON 03 DEC 2001)  
 DEL HIS Y

FILE 'HCAPLUS, WPIDS, MEDLINE, BIOSIS' ENTERED AT 10:04:53 ON 03 DEC 2001

E BAR OR D/AU  
 L1 93 S E3-4  
 E LAU E/AU  
 L2 469 S E3-23  
 L3 42 S E40-45  
 L4 585 S L1 OR L2 OR L3  
 L5 12 S L4 AND RADICAL?  
 L6 39 S L4 AND ALBUMIN?  
 L7 7 S L5 AND L6  
 L8 3 DUP REM L7 (4 DUPLICATES REMOVED)  
 L9 1161485 S OXYGEN OR OXIDATIVE?  
 L10 16 S L4 AND L9  
 L11 6 S L10 AND L6  
 L12 3 DUP REM L11 (3 DUPLICATES REMOVED)  
 L13 4 S L12 OR L8

=&gt; d all 1-13

L13 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2001 ACS  
 AN 2001:416050 HCAPLUS  
 DN 135:193981  
 TI An Analog of the Human **Albumin** N-Terminus (Asp-Ala-His-Lys)  
 Prevents Formation of Copper-Induced Reactive **Oxygen** Species  
 AU **Bar-Or, David**; Rael, Leonard T.; **Lau, Edward P.**; Rao,  
 Nagaraja K. R.; Thomas, Gregory W.; Winkler, James V.; Yukl, Richard L.;  
 Kingston, Robert G.; Curtis, C. Gerald  
 CS Department of Trauma Research, Swedish Medical Center, Englewood, CO,  
 80110, USA  
 SO Biochem. Biophys. Res. Commun. (2001), 284(3), 856-862  
 CODEN: BBRC99; ISSN: 0006-291X  
 PB Academic Press  
 DT Journal  
 LA English  
 CC 14-15 (Mammalian Pathological Biochemistry)  
 AB Copper mobilization and redox activity form damaging reactive oxygen  
 species (ROS) and are implicated in the pathogenesis of ischemia  
 -reperfusion injury, chronic inflammation, Alzheimer's disease, aging, and  
 cancer. Protein sequestration of Cu(II) ions has been shown to prevent  
 ROS-generating reactions. The first four amino acids of the N-terminus of  
 human albumin, Asp-Ala-His-Lys (DAHK), form a tight binding site for  
 Cu(II) ions. We synthesized several analogs, including the enantiomer  
 d-DAHK, to study their effects on copper-induced hydroxyl radical and  
 superoxide formation in the presence of ascorbate. D-DAHK prevented  
 thiobarbituric acid-reactive species (TBARS) formation within physiol. and  
 acidic pH ranges (7.5-6.5) and inhibited low-d. lipoprotein lipid  
 peroxidn. A d-DAHK/Cu complex exhibited superoxide dismutase-like  
 activity by significantly inhibiting superoxide formation. These in vitro  
 results suggest that d-DAHK may shift the Cu(II)-binding equil. from the  
 exchangeable Cu(II) pool to the tightly-bound, nonexchangeable pool,  
 prevent ROS formation, and potentially provide therapeutic benefit for  
 ROS-related diseases. (c) 2001 Academic Press.  
 ST human **albumin** N terminus copper induced reactive **oxygen**  
 species  
 IT **Albumins**, biological studies

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (N-terminus Asp-Ala-His-Lys; analog of human **albumin**  
 N-terminus (Asp-Ala-His-Lys) prevents formation of copper-induced  
 reactive **oxygen** species)

IT Protein motifs  
 (N-terminus of human **albumin**; analog of human **albumin**  
 N-terminus (Asp-Ala-His-Lys) prevents formation of copper-induced  
 reactive **oxygen** species)

IT Ischemia  
**Oxidative** stress, biological  
 (analog of human **albumin** N-terminus (Asp-Ala-His-Lys)  
 prevents formation of copper-induced reactive **oxygen** species)

IT Reactive **oxygen** species  
 RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence);  
 BIOL (Biological study); OCCU (Occurrence)  
 (analog of human **albumin** N-terminus (Asp-Ala-His-Lys)  
 prevents formation of copper-induced reactive **oxygen** species)

IT Reperfusion  
 (injury; analog of human **albumin** N-terminus (Asp-Ala-His-Lys)  
 prevents formation of copper-induced reactive **oxygen** species)

IT Disease, animal  
 (reactive **oxygen** species-related; analog of human  
**albumin** N-terminus (Asp-Ala-His-Lys) prevents formation of  
 copper-induced reactive **oxygen** species)

IT 7440-50-8, Copper, biological studies  
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
 (analog of human **albumin** N-terminus (Asp-Ala-His-Lys)  
 prevents formation of copper-induced reactive **oxygen** species)

IT 7782-44-7D, **Oxygen, radicals**  
 RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence);  
 BIOL (Biological study); OCCU (Occurrence)  
 (analog of human **albumin** N-terminus (Asp-Ala-His-Lys)  
 prevents formation of copper-induced reactive **oxygen** species)

IT 3352-57-6, Hydroxyl, biological studies 11062-77-4, Superoxide anion  
 RL: BOC (Biological occurrence); BPR (Biological process); BIOL  
 (Biological study); OCCU (Occurrence); PROC (Process)  
 (analog of human **albumin** N-terminus (Asp-Ala-His-Lys)  
 prevents formation of copper-induced reactive **oxygen** species)

IT 50-81-7, Ascorbic acid, biological studies 111543-77-2  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (analog of human **albumin** N-terminus (Asp-Ala-His-Lys)  
 prevents formation of copper-induced reactive **oxygen** species)

RE.CNT 52

RE

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L13 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2001 ACS

AN 2000:241618 HCAPLUS

DN 132:276296

TI ~~Tests and kits for the rapid evaluation of ischemic states by measuring altered serum albumins~~

IN ~~Bar-or, David; Lau, Edward; Winkler, James V.~~

PA Ischemia Technologies, Inc., USA

SO PCT Int. Appl., 105 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM G01N021-00

ICS G01N021-29; G01N031-22; G01N033-543; G01N033-00; G01N033-53;  
C12Q001-00

CC 9-5 (Biochemical Methods)

Section cross-reference(s): 14

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000020840	A1	20000413	WO 1999-US22905	19991001
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,				

MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,  
 SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ,  
 BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,  
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,  
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 AU 9964095 A1 20000426 AU 1999-64095 19991001  
 EP 1125107 A1 20010822 EP 1999-951710 19991001  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI  
 PRAI US 1998-102738 P 19981002  
 US 1998-165581 A2 19981002  
 US 1998-165926 A2 19981002  
 US 1999-115392 P 19990111  
 WO 1999-US22905 W 19991001  
 AB The present invention relates to rapid methods for the detection of  
 ischemic states and to kits for use in such methods. Provided for is a  
 rapid method of testing for and quantifying ischemia based upon methods of  
 detecting and quantifying the existence of an alteration of the serum  
 protein albumin which occurs following an ischemic event; methods for  
 detecting and quantifying this alteration include evaluating and  
 quantifying the cobalt binding capacity of circulating albumin, anal. and  
 measurement of the ability of serum albumin to bind exogenous cobalt,  
 detection and measurement of the presence of endogenous copper in a  
 purified albumin sample and use of an immunol. assay specific to the  
 altered form of serum albumin which occurs following an ischemic event.  
 Also taught by the present invention is the detection and measurement of  
 an ischemic event by measuring albumin N-terminal derivs. that arise  
 following an ischemic event, including truncated albumin species lacking  
 one to four N-terminal amino acids or albumin with an acetylated  
 N-terminal Asp residue. Patient sera was added to two tubes contg. CoCl<sub>2</sub>.  
 After reaction, dithiothreitol was added to one of the tubes and NaCl was  
 added to both. A470 spectroscopy measurements were taken of the two  
 tubes.  
 ST serum **albumin** detn ischemia; cobalt serum **albumin**  
 spectroscopy ischemia; copper serum **albumin** ischemia  
 IT Heart  
 (ECG; tests and kits for rapid evaluation of ischemic states by  
 measuring altered serum **albumins**)  
 IT Amniotic fluid  
 Biological materials  
 Body fluid  
 Cerebrospinal fluid  
 Lymph  
 Saliva  
 (anal. of; tests and kits for rapid evaluation of ischemic states by  
 measuring altered serum **albumins**)  
 IT Heart, disease  
 (angina pectoris; tests and kits for rapid evaluation of ischemic  
 states by measuring altered serum **albumins**)  
 IT Artery  
 (angioplasty, assessing efficacy of; tests and kits for rapid  
 evaluation of ischemic states by measuring altered serum  
**albumins**)  
 IT Heart, disease  
 (arrhythmia; tests and kits for rapid evaluation of ischemic states by  
 measuring altered serum **albumins**)  
 IT Calibration  
 (compn. for; tests and kits for rapid evaluation of ischemic states by  
 measuring altered serum **albumins**)

- IT Ligands  
RL: ARG (Analytical reagent use); DEV (Device component use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(immobilized, to **albumin**; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
- IT Antibodies  
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(immobilized; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
- IT Heart, disease  
(infarction; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
- IT Salts, biological studies  
RL: ARG (Analytical reagent use); RCT (Reactant); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(metal ion; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
- IT Antibodies  
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
(monoclonal, to human serum **albumin** N-terminal derivs.; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
- IT **Albumins**, analysis  
RL: ANT (Analyte); BOC (Biological occurrence); RCT (Reactant); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); USES (Uses)  
(serum; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
- IT Atomic absorption spectrometry  
Atomic emission spectrometry  
Blood analysis  
Color formers  
Diagnosis  
Exercise  
Filters  
Immunoassay  
Ischemia  
Test kits  
(tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
- IT Antibodies  
RL: ARG (Analytical reagent use); BPR (Biological process); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)  
(tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
- IT 263740-32-5, 5-585-Serum **albumin** (human) 263740-33-6, 3-585-Serum **albumin** (human) 263740-34-7, 2-585-Serum **albumin** (human) 263740-35-8, Serum **albumin** (human) 263740-36-9, 4-585-Serum **albumin** (human)  
RL: ANT (Analyte); BPR (Biological process); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process)  
(amino acid sequence, monoclonal antibody to N-terminus of; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
- IT 111543-77-2D, salts or complexes  
RL: ARG (Analytical reagent use); BPR (Biological process); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC

- (Process); USES (Uses)  
(antibody to or color-forming compds. contg.; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
- IT 7782-44-7, **Oxygen**, processes  
RL: PEP (Physical, engineering or chemical process); PROC (Process)  
(cobalt binding to octapeptide enhancement by; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
- IT 263562-84-1  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); PROC (Process)  
(cobalt ion reactivity with; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
- IT 263562-85-2P 263562-86-3P  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)  
(cobalt ion reactivity with; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
- IT 541-50-4D, derivs. 13598-36-2D, Phosphonic acid, derivs.  
RL: DEV (Device component use); USES (Uses)  
(matrix, as support; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
- IT 111543-77-2  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)  
(nickel and copper ions reactivity with; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
- IT 263562-87-4 263562-88-5 263562-89-6  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)  
(nickel ion reactivity with; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
- IT 7440-50-8D, Copper, salts or ions or complexes with human serum **albumin**  
RL: ANT (Analyte); ARG (Analytical reagent use); BPR (Biological process); RCT (Reactant); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)  
(tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
- IT 7646-79-9, Cobalt chloride, biological studies 7718-54-9, Nickel chloride, biological studies 7758-98-7, Sulfuric acid copper(2+) salt (1:1), biological studies  
RL: ARG (Analytical reagent use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)  
(tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
- IT 7439-89-6D, Iron, salts 7439-92-1D, Lead, salts 7439-96-5D, Manganese, salts 7439-97-6D, Mercury, salts 7439-98-7D, Molybdenum, salts 7440-02-0D, Nickel, salts or support-immobilized 7440-22-4D, Silver, salts 7440-36-0D, Antimony, salts 7440-38-2D, Arsenic, salts 7440-39-3D, Barium, salts 7440-43-9D, Cadmium, salts 7440-47-3D, Chromium, salts 7440-48-4D, Cobalt, salts or support-immobilized 7440-57-5D, Gold, salts 7440-62-2D, Vanadium, salts 7440-66-6D, Zinc, salts  
RL: ARG (Analytical reagent use); RCT (Reactant); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT 134872-38-1  
 RL: PRP (Properties); RCT (Reactant)  
 (tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT 263562-90-9P  
 RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
 (tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

RE.CNT 2  
 RE  
 (1) Bar-Or; US 5227307 A 1993  
 (2) Bar-Or; US 5290519 A 1994

L13 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2001 ACS

AN 2000:241285 HCAPLUS

DN 132:276307

TI Methods and materials for detection and measurement of free radical damage

IN Bar-Or, David; Lau, Edward

PA Diagnostic Markers, Inc., USA

SO PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K014-47

ICS C07K016-06; G01N033-534

CC 9-16 (Biochemical Methods)

Section cross-reference(s): 1, 14

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020454	A1	20000413	WO 1999-US22746	19991001
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9962793	A1	20000426	AU 1999-62793	19991001
EP 1117686	A1	20010725	EP 1999-950055	19991001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI US 1998-102962	P	19981002		
US 1998-165961	A	19981002		
WO	W	19991001		

AB The mea  
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a marker useful for detection and specifically, the invention takes the N-terminus of the albumin good, in the presence of free ability of the N-terminus of the for detecting and quantifying this tifying the cobalt binding capacity measurement of the ability of ction and measurement of the in sample and use of an immunol.

assay specific to the altered form of serum albumin which occurs following free radical damage. Also taught by the present invention is the use of the peptide Asp Ala His Lys and the compd. Asp-Ala-His-Lys-R, wherein R is any chem. group capable of producing a detectable signal when a metal ion capable of binding to the N-terminus of naturally-occurring albumin is bound to the compd., for detection and quantitation of the marker. Methods of the present invention also include use of the marker as a "biochem. tag", thereby allowing for sensitive detection and measurement of the efficacy of clin. drugs and therapeutics which result in the generation of free radicals or which act to limit free radical damage. The marker also acts as a "biol. tag" of a process implicated in a wide array of diseases and conditions and, accordingly, may be used to monitor and assess such diseases and conditions. Finally, the invention provides antibodies, immunoassays, and kits for use in detecting or quantitating the marker.

- ST detection free **radical** damage
- IT **Radicals**, biological studies
  - RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (damage; methods and materials for detection and measurement of free **radical** damage)
- IT Transition metals, biological studies
  - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ions; methods and materials for detection and measurement of free **radical** damage)
- IT Atomic absorption spectrometry
  - Atomic emission spectrometry
  - Containers
  - Disease, animal
  - Drugs
  - Immunoassay
  - Test kits
  - Therapy
    - (methods and materials for detection and measurement of free **radical** damage)
- IT Antibodies
  - RL: ANT (Analyte); ANST (Analytical study) (methods and materials for detection and measurement of free **radical** damage)
- IT **Albumins**, biological studies
  - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (methods and materials for detection and measurement of free **radical** damage)
- IT Metals, biological studies
  - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (methods and materials for detection and measurement of free **radical** damage)
- IT Peptides, biological studies
  - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (methods and materials for detection and measurement of free **radical** damage)
- IT Periodic system
  - (salt of transition metal ions; methods and materials for detection and measurement of free **radical** damage)
- IT **Albumins**, biological studies
  - Albumins**, biological studies
  - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (serum; methods and materials for detection and measurement of free **radical** damage)
- IT 7439-89-6D, Iron, salts    7439-92-1D, Lead, salts    7439-96-5D, Manganese, salts    7439-97-6D, Mercury, salts    7439-98-7D, Molybdenum, salts



7440-02-0D, Nickel, salts 7440-22-4D, Silver, salts 7440-36-0D, Antimony, salts 7440-38-2D, Arsenic, salts 7440-39-3D, Barium, salts 7440-43-9D, Cadmium, salts 7440-47-3D, Chromium, salts 7440-48-4, Cobalt, biological studies 7440-48-4D, Cobalt, salts 7440-50-8D, Copper, salts 7440-57-5D, Gold, salts 7440-62-2D, Vanadium, salts 7440-66-6D, Zinc, salts 111543-77-2, Asp-Ala-His-Lys

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methods and materials for detection and measurement of free radical damage)

IT 134872-38-1 263698-69-7

RL: PRP (Properties)  
(unclaimed sequence; methods and materials for detection and measurement of free radical damage)

RE.CNT 3

RE

- (1) Cotellet, N; Journal of Inorganic Biochemistry 1992, V46, P7 HCAPLUS
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- (3) Laussac, J; Biochemistry 1984, V23(12), P2832 HCAPLUS

L13 ANSWER 4 OF 4 MEDLINE

AN 2001166045 MEDLINE

DN 21164743 PubMed ID: 11264015

TI Asp-Ala-His-Lys (DAHK) inhibits copper-induced oxidative DNA double strand breaks and telomere shortening.

AU Bar-Or D; Thomas G W; Rael L T; Lau E P; Winkler J V

CS Trauma Research, Swedish Medical Center, Englewood, Colorado, 80110, USA..  
dbaror@dmibio.com

SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2001 Mar 23) 282 (1) 356-60.

Journal code: 9Y8; 0372516. ISSN: 0006-291X.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200104

ED Entered STN: 20010417

Last Updated on STN: 20010417

Entered Medline: 20010412

AB Both DNA and the telomeric sequence are susceptible to copper-mediated reactive oxygen species (ROS) damage, particularly damage attributed to hydroxyl radicals. In this study, ROS-induced DNA double strand breaks and telomere shortening were produced by exposure to copper and ascorbic acid. Asp-Ala-His-Lys (DAHK), a specific copper chelating tetrapeptide d-analog of the N-terminus of human albumin, attenuated DNA strand breaks in a dose dependent manner. d-DAHK, at a ratio of 4:1 (d-DAHKCu), provided complete protection of isolated DNA from double strand breaks and, at a ratio of 2:1 (d-DAHKCu), completely protected DNA in Raji cells exposed to copper/ascorbate. Southern blots of DNA treated with copper/ascorbate showed severe depletion and shortening of telomeres and Raji cell treated samples showed some conservation of telomere sequences. d-DAHK provided complete telomere length protection at a ratio of 2:1 (d-DAHKCu). The human albumin N-terminus analog, d-DAHK, protects DNA and telomeres against copper-mediated ROS damage and may be a useful therapeutic adjunct in ROS disease processes. Copyright 2001 Academic Press.

CT Check Tags: Human; Support, Non-U.S. Gov't  
Cell Line

\*Copper: AI, antagonists & inhibitors

Copper: PD, pharmacology

DNA: DE, drug effects

Shah 09/820,416

\*DNA Damage

\*Oligopeptides: PD, pharmacology

**\*Oxidative Stress**

\*Telomere: DE, drug effects

RN 7440-50-8 (Copper); 9007-49-2 (DNA)

CN 0 (Oligopeptides)

=&gt; d his

*sequence search on STN*

(FILE 'WPIDS' ENTERED AT 09:31:09 ON 03 DEC 2001)  
DEL HIS Y

FILE 'REGISTRY' ENTERED AT 09:33:11 ON 03 DEC 2001

L1 88 S ^DAHK/SQSP  
L2 19 S L1 AND SQL=4

FILE 'HCAPLUS' ENTERED AT 09:34:32 ON 03 DEC 2001

L3 13 S L2  
L4 4 S L3 AND RADICAL?  
L5 4 S L1 AND RADICAL?  
L6 4 S L4 OR L5

=&gt; d .ca 16 1-4

L6 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:416050 HCAPLUS

DOCUMENT NUMBER: 135:193981

TITLE: An Analog of the Human Albumin N-Terminus  
(Asp-Ala-His-Lys) Prevents Formation of Copper-Induced  
Reactive Oxygen Species

AUTHOR(S): Bar-Or, David; Rael, Leonard T.; Lau, Edward P.; Rao,  
Nagaraja K. R.; Thomas, Gregory W.; Winkler, James V.;  
Yukl, Richard L.; Kingston, Robert G.; Curtis, C.  
Gerald

CORPORATE SOURCE: Department of Trauma Research, Swedish Medical Center,  
Englewood, CO, 80110, USA

SOURCE: Biochem. Biophys. Res. Commun. (2001), 284(3), 856-862  
CODEN: BBRC99; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Copper mobilization and redox activity form damaging reactive oxygen species (ROS) and are implicated in the pathogenesis of ischemia-reperfusion injury, chronic inflammation, Alzheimer's disease, aging, and cancer. Protein sequestration of Cu(II) ions has been shown to prevent ROS-generating reactions. The first four amino acids of the N-terminus of human albumin, Asp-Ala-His-Lys (DAHK), form a tight binding site for Cu(II) ions. We synthesized several analogs, including the enantiomer d-DAHK, to study their effects on copper-induced hydroxyl radical and superoxide formation in the presence of ascorbate. D-DAHK prevented thiobarbituric acid-reactive species (TBARS) formation within physiolo. and acidic pH ranges (7.5-6.5) and inhibited low-d. lipoprotein lipid peroxidn. A d-DAHK/Cu complex exhibited superoxide dismutase-like activity by significantly inhibiting superoxide formation. These in vitro results suggest that d-DAHK may shift the Cu(II)-binding equil. from the exchangeable Cu(II) pool to the tightly-bound, nonexchangeable pool, prevent ROS formation, and potentially provide therapeutic benefit for ROS-related diseases. (c) 2001 Academic Press.

CC 14-15 (Mammalian Pathological Biochemistry)

IT 7782-44-7D, Oxygen, radicals

RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence);  
BIOL (Biological study); OCCU (Occurrence)

(analog of human albumin N-terminus (Asp-Ala-His-Lys) prevents  
formation of copper-induced reactive oxygen species)

IT 50-81-7, Ascorbic acid, biological studies 111543-77-2

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(analog of human albumin N-terminus (Asp-Ala-His-Lys) prevents formation of copper-induced reactive oxygen species)

REFERENCE COUNT: 52

REFERENCE(S): (1) Athar, M; Biochem Mol Biol Int 1996, V39, P813 HCAPLUS  
(2) Bar-Or, D; Am Heart J 2001, V141, P985 HCAPLUS  
(3) Bar-Or, D; Eur J Biochem 2001, V268, P42 HCAPLUS  
(5) Beauchamp, C; Anal Biochem 1971, V44, P276 HCAPLUS  
(6) Belayev, L; Stroke 2001, V32, P553 HCAPLUS  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:265447 HCAPLUS

DOCUMENT NUMBER: 134:290423

TITLE: Metal-binding peptide compounds for reducing the damage done by reactive oxygen species and reducing the concn. of a metal in an animal

INVENTOR(S): Bar-Or, David; Curtis, C. Gerald; Lau, Edward; Rao, Nagaraja K. R.; Winkler, James V.; Crook, Wannell M.

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 124 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001025265	A1	20010412	WO 2000-US26952	20000929
<p>W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM</p> <p>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG</p>				

PRIORITY APPLN. INFO.: US 1999-157404 P 19991001

US 2000-211078 P 20000613

AB A method is provided for reducing the damage done by reactive oxygen species (ROS) in an animal. The invention also provides a method of reducing the concn. of a metal in an animal. These methods comprise administering to the animal an effective amt. of a metal-binding peptide compd. The invention further provides a method of reducing the damage done by ROS in a tissue or an organ that has been removed from an animal. The method comprises contacting the tissue or organ with a soln. contg. an effective amt. of a metal-binding peptide compd. of the invention. The invention further provides metal-binding peptide compds., pharmaceutical compns., and kits.

IC ICM C07K007-00

CC 1-12 (Pharmacology)

Section cross-reference(s): 34, 63

IT 3352-57-6, Hydroxyl radical, biological studies

RL: ADV (Adverse effect, including toxicity); BPR (Biological process);

MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)

(metal-binding peptide compds. for redn. of damage done by reactive oxygen species and redn. of concn. of metal in animal)

IT 71-00-1, Histidine, biological studies 111543-77-2D, copper complexes  
 RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)  
 (metal-binding peptide compds. for redn. of damage done by reactive oxygen species and redn. of concn. of metal in animal)

IT 111543-77-2P  
 RL: BAC (Biological activity or effector, except adverse); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (metal-binding peptide compds. for redn. of damage done by reactive oxygen species and redn. of concn. of metal in animal)

IT 263562-85-2 263562-86-3 263562-87-4 263562-88-5  
 RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (metal-binding peptide compds. for redn. of damage done by reactive oxygen species and redn. of concn. of metal in animal)

IT 333952-24-2P  
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (metal-binding peptide compds. for redn. of damage done by reactive oxygen species and redn. of concn. of metal in animal)

IT 81748-02-9P 333952-21-9P 333952-22-0P 333952-23-1P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (metal-binding peptide compds. for redn. of damage done by reactive oxygen species and redn. of concn. of metal in animal)

REFERENCE COUNT: 1

REFERENCE(S): (1) Pallenberg; US 5538945 A 1996 HCAPLUS

L6 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:241285 HCAPLUS

DOCUMENT NUMBER: 132:276307

TITLE: Methods and materials for detection and measurement of free radical damage

INVENTOR(S): Bar-Or, David; Lau, Edward

PATENT ASSIGNEE(S): Diagnostic Markers, Inc., USA

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020454	A1	20000413	WO 1999-US22746	19991001
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9962793	A1	20000426	AU 1999-62793	19991001
EP 1117686	A1	20010725	EP 1999-950055	19991001

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.:

US 1998-102962 P 19981002

US 1998-165961 A 19981002

WO 1999-US22746 W 19991001

- AB The present invention teaches a marker useful for detection and measurement of free radical damage. Specifically, the invention takes advantage of alterations which occur to the N-terminus of the albumin mol., a circulating protein in human blood, in the presence of free radicals. These alterations effect the ability of the N-terminus of the albumin mol. to bind metals. Methods for detecting and quantifying this alteration include evaluating and quantifying the cobalt binding capacity of an albumin-contg. sample, anal. and measurement of the ability of albumin to bind exogenous cobalt, detection and measurement of the presence of copper in a purified albumin sample and use of an immunol. assay specific to the altered form of serum albumin which occurs following free radical damage. Also taught by the present invention is the use of the peptide Asp Ala His Lys and the compd. Asp-Ala-His-Lys-R, wherein R is any chem. group capable of producing a detectable signal when a metal ion capable of binding to the N-terminus of naturally-occurring albumin is bound to the compd., for detection and quantitation of the marker. Methods of the present invention also include use of the marker as a "biochem. tag", thereby allowing for sensitive detection and measurement of the efficacy of clin. drugs and therapeutics which result in the generation of free radicals or which act to limit free radical damage. The marker also acts as a "biol. tag" of a process implicated in a wide array of diseases and conditions and, accordingly, may be used to monitor and assess such diseases and conditions. Finally, the invention provides antibodies, immunoassays, and kits for use in detecting or quantitating the marker.
- IC ICM C07K014-47  
ICS C07K016-06; G01N033-534
- CC 9-16 (Biochemical Methods)  
Section cross-reference(s): 1, 14
- ST detection free **radical** damage
- IT **Radicals**, biological studies  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(damage; methods and materials for detection and measurement of free **radical** damage)
- IT Transition metals, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ions; methods and materials for detection and measurement of free **radical** damage)
- IT Atomic absorption spectrometry  
Atomic emission spectrometry  
Containers  
Disease, animal  
Drugs  
Immunoassay  
Test kits  
Therapy  
(methods and materials for detection and measurement of free **radical** damage)
- IT Antibodies  
RL: ANT (Analyte); ANST (Analytical study)  
(methods and materials for detection and measurement of free **radical** damage)
- IT Albumins, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methods and materials for detection and measurement of free

- radical damage)
- IT Metals, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methods and materials for detection and measurement of free radical damage)
- IT Peptides, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methods and materials for detection and measurement of free radical damage)
- IT Periodic system  
(salt of transition metal ions; methods and materials for detection and measurement of free radical damage)
- IT Albumins, biological studies  
Albumins, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(serum; methods and materials for detection and measurement of free radical damage)
- IT 7439-89-6D, Iron, salts 7439-92-1D, Lead, salts 7439-96-5D, Manganese, salts 7439-97-6D, Mercury, salts 7439-98-7D, Molybdenum, salts 7440-02-0D, Nickel, salts 7440-22-4D, Silver, salts 7440-36-0D, Antimony, salts 7440-38-2D, Arsenic, salts 7440-39-3D, Barium, salts 7440-43-9D, Cadmium, salts 7440-47-3D, Chromium, salts 7440-48-4, Cobalt, biological studies 7440-48-4D, Cobalt, salts 7440-50-8D, Copper, salts 7440-57-5D, Gold, salts 7440-62-2D, Vanadium, salts 7440-66-6D, Zinc, salts 111543-77-2, Asp-Ala-His-Lys  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methods and materials for detection and measurement of free radical damage)
- IT 134872-38-1 263698-69-7  
RL: PRP (Properties)  
(unclaimed sequence; methods and materials for detection and measurement of free radical damage)

## REFERENCE COUNT:

## REFERENCE(S):

- (1) Cotellet, N; Journal of Inorganic Biochemistry 1992, V46, P7 HCAPLUS
- (2) Keller, R; Chem Res Toxicol 1993, V6(4), P430 HCAPLUS
- (3) Laussac, J; Biochemistry 1984, V23(12), P2832 HCAPLUS

L6 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1992:402510 HCAPLUS

DOCUMENT NUMBER: 117:2510

TITLE: Redox chemistry of complexes of nickel(II) with some biologically important peptides in the presence of reduced oxygen species: an ESR study

AUTHOR(S): Cotellet, N.; Tremolieres, E.; Bernier, J. L.; Catteau, J. P.; Henichart, J. P.

CORPORATE SOURCE: INSERM, Lille, 59045, Fr.

SOURCE: J. Inorg. Biochem. (1992), 46(1), 7-15  
CODEN: JIBIDJ; ISSN: 0162-0134

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The reactions between some Ni(II) oligopeptides (Gly-His-Lys, (Gly)<sub>4</sub>, Asp-Ala-His-Lys, Gly-Gly-His, .beta.Ala-His, and serum albumin) and reduced oxygen species were characterized by spin-trapping expts. using DMPO and Me<sub>2</sub>SO. Most of the peptides possessed superoxide dismutase- and catalase-like activities leading to the formation of either oxene [NiO]<sub>2</sub><sup>+</sup> or, in the case of .beta.Ala-His, hydroxyl radicals. Both these species may affect DNA integrity through distinct mechanisms.

CC 4-6 (Toxicology)  
 IT 3352-57-6, Hydroxylradical, reactions 7722-84-1, Hydrogen peroxide,  
 biological studies 7782-44-7D, Oxygen, **radicals** 11062-77-4,  
 Superoxide anion  
 RL: RCT (Reactant)  
 (reaction of, with nickel-oligopeptide complexes)  
 IT 305-84-0D, nickel complexes 7440-02-0D, Nickel, oligopeptide complexes  
 7451-76-5D, nickel complexes 39016-92-7 49557-75-7D, nickel complexes  
**111543-77-2D**, nickel complexes  
 RL: RCT (Reactant)  
 (reaction of, with reactive oxygen species)

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 E49 THROUGH E56 ASSIGNED

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STRUCTURE FILE UPDATES: 30 NOV 2001 HIGHEST RN 372937-30-9  
 DICTIONARY FILE UPDATES: 30 NOV 2001 HIGHEST RN 372937-30-9

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when  
 conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES  
 for more information. See STNote 27, Searching Properties in the CAS  
 Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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 (134872-38-1/RN)  
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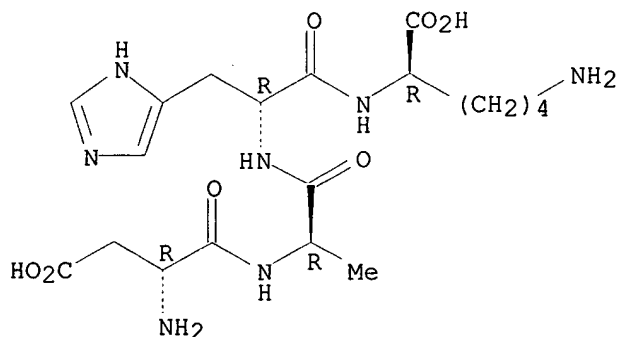
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RN 333952-24-2 REGISTRY  
CN D-Lysine, D-.alpha.-aspartyl-D-alanyl-D-histidyl- (9CI) (CA INDEX NAME)  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL 4

SEQ3 1 Asp-Ala-His-Lys  
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MF C19 H31 N7 O7  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L8 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2001 ACS  
RN 333952-23-1 REGISTRY  
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NTE modified

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modification	Lys-4	undetermined modification

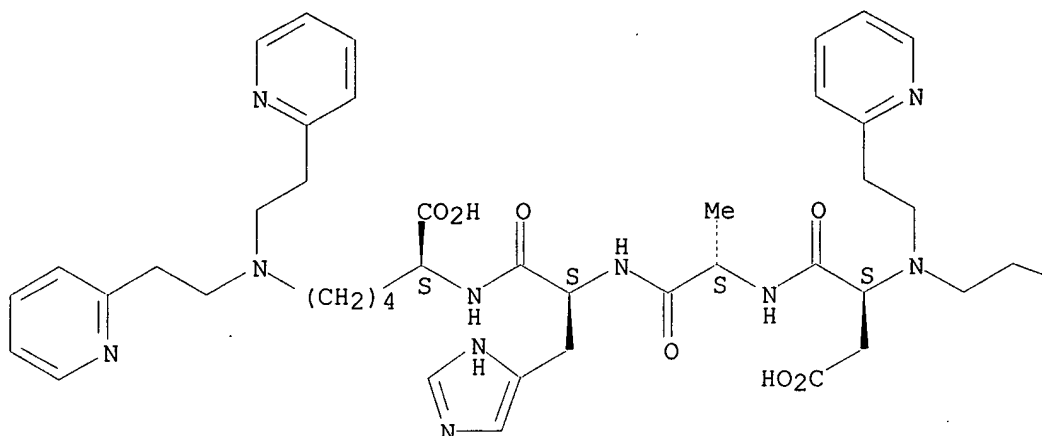
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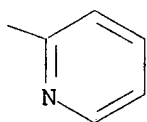
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Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L8 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2001 ACS  
 RN 333952-22-0 REGISTRY  
 CN L-Lysine, 4,4'-[(7,12-diethyl-3,8,13,17-tetramethyl-21H,23H-porphine-2,18-diyl)bis(1-oxo-3,1-propanediyl)]bis[L.alpha.-aspartyl-L-alanyl-L-histidyl-  
 (9CI) (CA INDEX NAME)  
 FS PROTEIN SEQUENCE; STEREOSEARCH  
 SQL 8,4,4  
 NTE multichain  
 modified (modifications unspecified)

type	location	description
bridge	Lys-4 - Lys-4'	covalent bridge, dimer

SEQ3 1 Asp-Ala-His-Lys

HITS AT: 1-4

SEQ3 1 Asp-Ala-His-Lys

HITS AT: 1-4

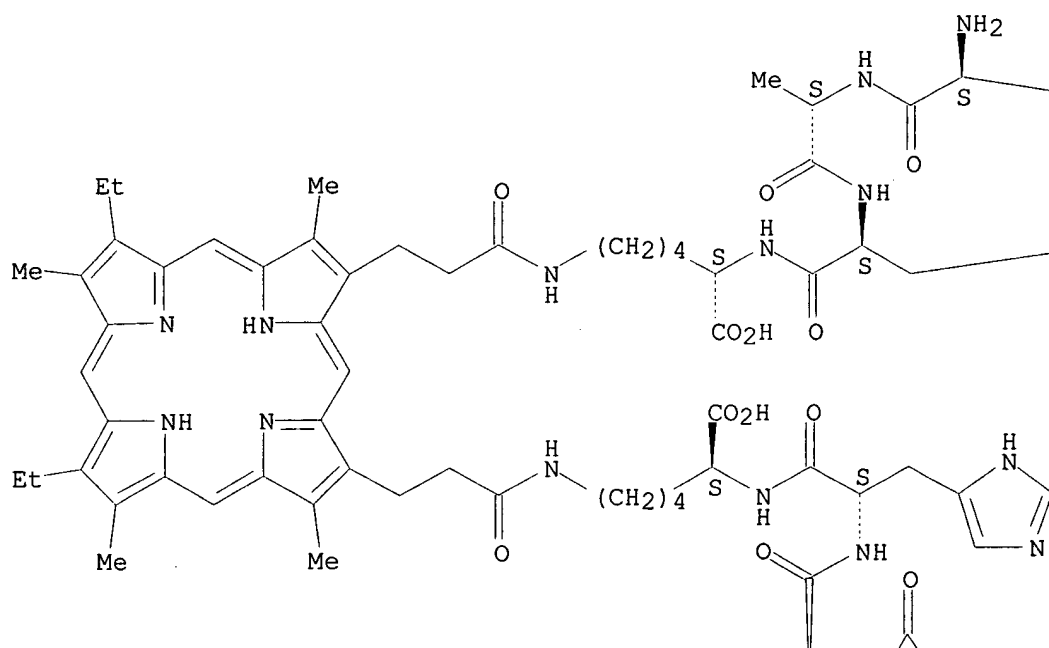
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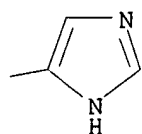
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Absolute stereochemistry.

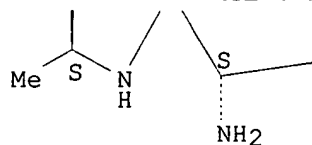
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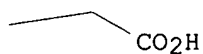
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PAGE 2-A



PAGE 2-B



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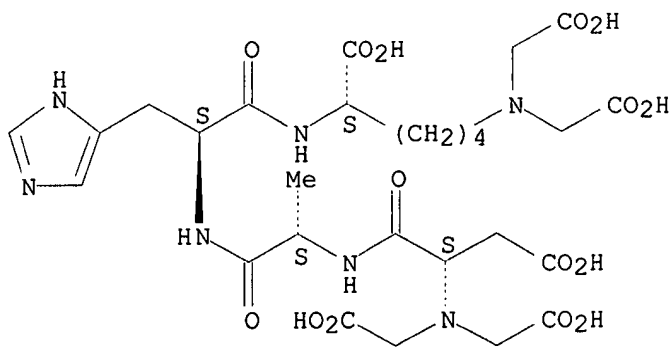
L8 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2001 ACS  
RN 333952-21-9 REGISTRY  
CN L-Lysine, N,N-bis(carboxymethyl)-L-.alpha.-aspartyl-L-alanyl-L-histidyl-  
N6,N6-bis(carboxymethyl)- (9CI) (CA INDEX NAME)  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL 4  
NTE modified (modifications unspecified)

SEQ3 1 Asp-Ala-His-Lys  
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HITS AT: 1-4

MF C27 H39 N7 O15  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L8 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2001 ACS  
RN 263562-86-3 REGISTRY  
CN L-Lysine, N-acetyl-L-.alpha.-aspartyl-L-alanyl-L-histidyl-L-lysyl-L-seryl-  
L-.alpha.-glutamyl-L-valyl-L-alanyl-L-histidyl-L-arginyl-L-phenylalanyl-  
(9CI) (CA INDEX NAME)

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 SQL 12  
 NTE modified

type	----- location -----	description
terminal mod.	Asp-1 -	N-acetyl

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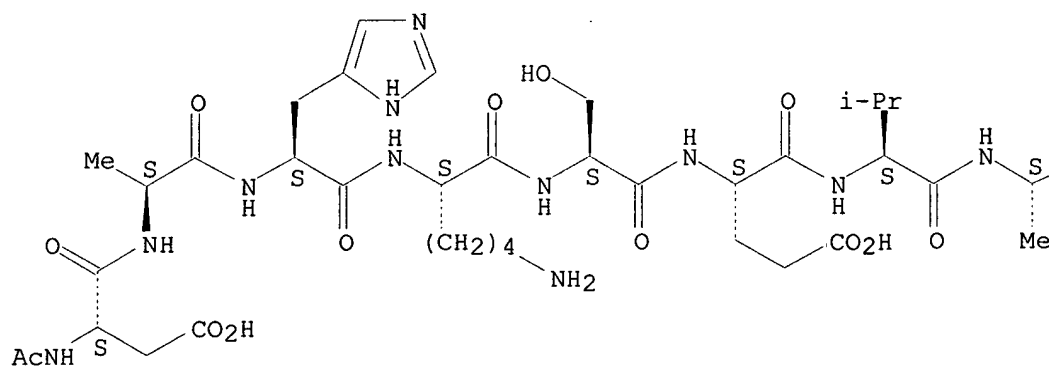
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SR CA

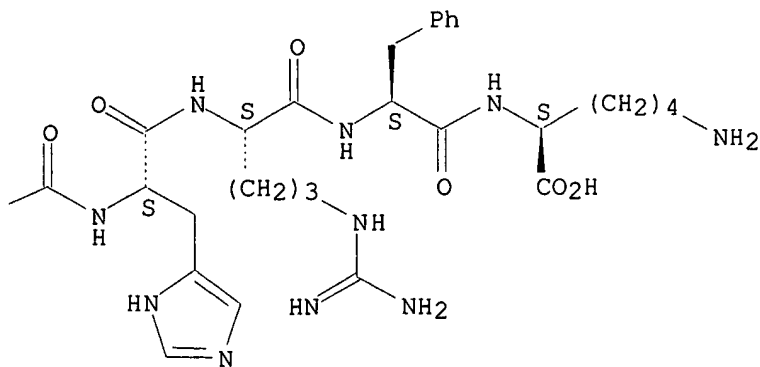
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



2 REFERENCES IN FILE CA (1967 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L8 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2001 ACS  
 RN 263562-85-2 REGISTRY  
 CN L-Lysine, L-.alpha.-aspartyl-L-alanyl-L-histidyl-L-lysyl-L-seryl-L-.alpha.-glutamyl-L-valyl-L-alanyl-L-histidyl-L-arginyl-L-phenylalanyl- (9CI) (CA INDEX NAME)  
 FS PROTEIN SEQUENCE; STEREOSEARCH  
 SQL 12

SEQ3 1 Asp-Ala-His-Lys-Ser-Glu-Val-Ala-His-Arg-  
 === === === ===

11 Phe-Lys

HITS AT: 1-4

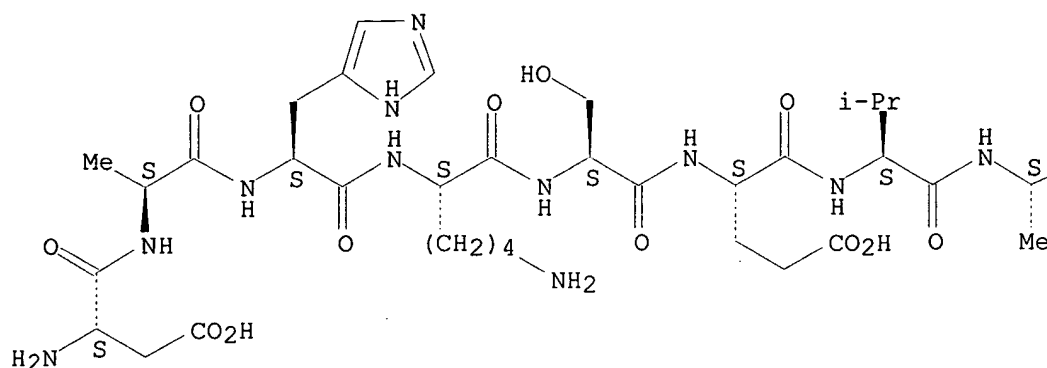
MF C62 H97 N21 O18

SR CA

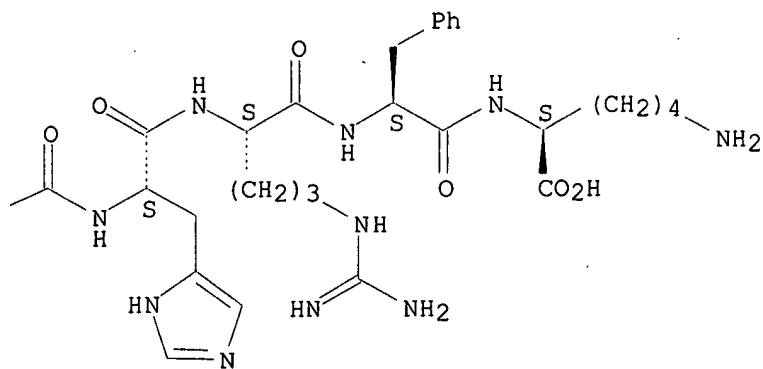
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



2 REFERENCES IN FILE CA (1967 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

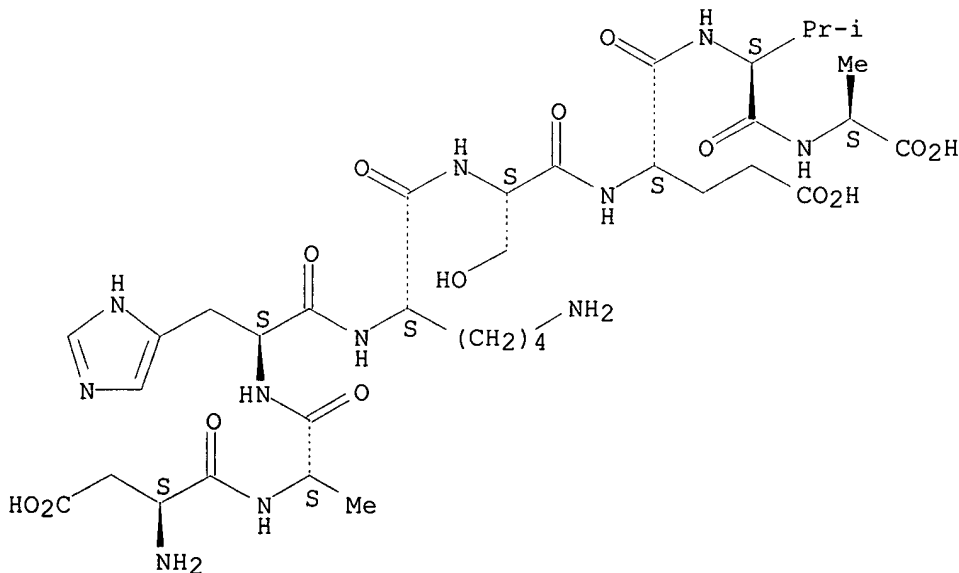
L8 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2001 ACS  
 RN 134872-38-1 REGISTRY  
 CN L-Alanine, L-.alpha.-aspartyl-L-alanyl-L-histidyl-L-lysyl-L-seryl-L-.alpha.-glutamyl-L-valyl- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN L-Alanine, N-[N-[N-[N2-[N-(N-L-.alpha.-aspartyl-L-alanyl)-L-histidyl]-L-lysyl]-L-seryl]-L-.alpha.-glutamyl]-L-valyl]-  
 OTHER NAMES:  
 CN 1: PN: WO0020454 SEQID: 2 unclaimed sequence  
 FS PROTEIN SEQUENCE; STEREOSEARCH  
 SQL 8

SEQ3 1 Asp-Ala-His-Lys-Ser-Glu-Val-Ala  
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HITS AT: 1-4

MF C35 H57 N11 O14  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



3 REFERENCES IN FILE CA (1967 TO DATE)  
 3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L8 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2001 ACS  
 RN 111543-77-2 REGISTRY  
 CN L-Lysine, L-.alpha.-aspartyl-L-alanyl-L-histidyl- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN L-Lysine, N2-[N-(N-L-.alpha.-aspartyl-L-alanyl)-L-histidyl]-  
 OTHER NAMES:  
 CN 1: PN: WO0020454 SEQID: 1 claimed protein  
 CN Asp-Ala-His-Lys  
 FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 4

SEQ3 1 Asp-Ala-His-Lys

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HITS AT: 1-4

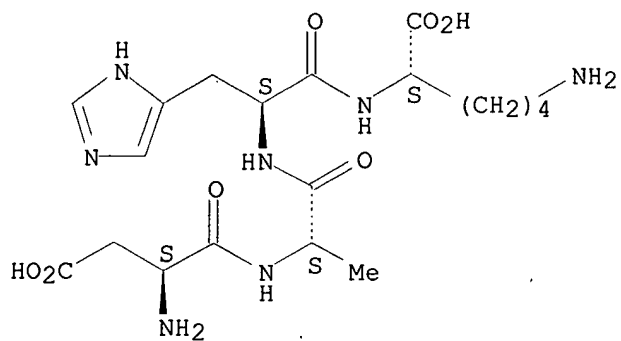
MF C19 H31 N7 O7

CI COM

SR CA

LC STN Files: CA, CAPLUS, CASREACT, CHEMCATS, TOXCENTER, TOXLIT

Absolute stereochemistry.



9 REFERENCES IN FILE CA (1967 TO DATE)

4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

9 REFERENCES IN FILE CAPLUS (1967 TO DATE)



=> d his

(FILE 'HOME' ENTERED AT 09:17:54 ON 03 DEC 2001)

FILE 'HCAPLUS' ENTERED AT 09:18:14 ON 03 DEC 2001

L1 139581 S RADICAL#  
L2 27616 S L1 (L) FREE  
L3 2911 S L1 (L) DAMAG?  
L4 59348 S ALBUMIN?  
L5 124 S L2 AND L4  
L6 58 S L3 AND L4  
L7 124 S L5 OR L5  
L8 162 S L5 OR L6  
L9 1090728 S METAL?  
L10 11 S L9 AND L8

FILE 'REGISTRY' ENTERED AT 09:20:13 ON 03 DEC 2001

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L11 1 S E3  
E PORFIMER SODIUM/CN  
L12 1 S E3

FILE 'HCAPLUS' ENTERED AT 09:21:14 ON 03 DEC 2001

L13 475 S L12 OR PORFIRMER?  
L14 0 S L13 AND L8  
L15 156256 S ANTIBOD?  
L16 49177 S ATOMIC (L) SPECT?  
L17 1 S L16 AND L8  
L18 7 S L15 AND L8  
L19 12045 S KIT#  
L20 111553 S IMMUNOASSAY? OR ASSAY?  
L21 5 S L8 AND (L19 OR L20)  
L22 19 S L10 OR L17 OR L18 OR L21  
L23 68 S L4 (L) L2  
L24 7 S L23 (L) DAMAG?  
L25 25 S L24 OR L22

=> fil hcaplus  
FILE 'HCAPLUS' ENTERED AT 09:24:29 ON 03 DEC 2001  
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FILE COVERS 1947 - 3 Dec 2001 VOL 135 ISS 24  
FILE LAST UPDATED: 2 Dec 2001 (20011202/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

HCAplus now provides online access to patents and literature covered in CA from 1947 to the present. On April 22, 2001, bibliographic information and abstracts were added for over 2.2 million references published in CA from 1947 to 1966.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

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(FILE 'HOME' ENTERED AT 09:17:54 ON 03 DEC 2001)

FILE 'HCAPLUS' ENTERED AT 09:18:14 ON 03 DEC 2001

L1 139581 S RADICAL#  
L2 27616 S L1 (L) FREE  
L3 2911 S L1 (L) DAMAG?  
L4 59348 S ALBUMIN?  
L5 124 S L2 AND L4  
L6 58 S L3 AND L4  
L7 124 S L5 OR L5  
L8 162 S L5 OR L6  
L9 1090728 S METAL?  
L10 11 S L9 AND L8

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L11 1 S E3  
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FILE 'HCAPLUS' ENTERED AT 09:21:14 ON 03 DEC 2001

L13 475 S L12 OR PORFIRMER?  
L14 0 S L13 AND L8  
L15 156256 S ANTIBOD?  
L16 49177 S ATOMIC (L) SPECT?  
L17 1 S L16 AND L8  
L18 7 S L15 AND L8

L19 12045 S KIT#  
 L20 111553 S IMMUNOASSAY? OR ASSAY?  
 L21 5 S L8 AND (L19 OR L20)  
 L22 19 S L10 OR L17 OR L18 OR L21  
 L23 68 S L4 (L) L2  
 L24 7 S L23 (L) DAMAG?  
 L25 25 S L24 OR L22

FILE 'HCAPLUS' ENTERED AT 09:24:29 ON 03 DEC 2001

=> d .ca 1-25

L25 ANSWER 1 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:293373 HCAPLUS

DOCUMENT NUMBER: 134:362454

TITLE: Structural damage to proteins caused by free radicals: assessment, protection by antioxidants, and influence of protein binding

AUTHOR(S): Salvi, A.; Carrupt, P.-A.; Tillement, J.-P.; Testa, B.

CORPORATE SOURCE: Section de Pharmacie, Institut de Chimie  
 Therapeutique, Universite de Lausanne, Lausanne,  
 CH-1015, Switz.

SOURCE: Biochem. Pharmacol. (2001), 61(10), 1237-1242

CODEN: BCPA6; ISSN: 0006-2952

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Oxidative damage to proteins results in biol. dysfunctions such as perturbed activity in enzymes, transport proteins, and receptors. Here, the authors investigated structural damage to proteins induced by free radicals. Structural alterations to lysozyme, human serum albumin (HSA) and .beta.-lactoglobulin A were monitored by capillary zone electrophoresis. Four well-known antioxidants (quercetin, melatonin, Trolox, and chlorogenic acid) were examd. for their ability to inhibit protein damage and to bind to these proteins. Melatonin and chlorogenic acid, which did not bind to any of the three proteins under study, showed scavenging and protective activities well correlated with the amt. of free radicals generated. Trolox, which bound only to HSA, was a better protector of HSA than of the two other proteins, indicating that its antioxidant capacity is increased by a shielding effect. Finally, quercetin was a good antioxidant in protecting lysozyme and .beta.-lactoglobulin A, but its binding to HSA resulted in a pro-oxidant effect that accelerated HSA fragmentation. These results demonstrate that binding of an antioxidant to a protein may potentiate protection or damage depending on the properties of the antioxidant.

CC 4-3 (Toxicology)

IT **Albumins**, biological studies

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(serum; structural **damage** to proteins caused by **free**

**radicals**: assessment, protection by antioxidants, and influence of protein binding)

REFERENCE COUNT: 18

REFERENCE(S): (1) Ahmed, M; Carcinogenesis 1994, V15, P1627 HCAPLUS  
 (2) Born, M; Helv Chim Acta 1996, V79, P1147 HCAPLUS  
 (3) Cao, G; Free Radic Biol Med 1997, V22, P749 HCAPLUS  
 (4) Davies, K; J Biol Chem 1987, V262, P8227 HCAPLUS  
 (5) Dean, R; Free Radic Res Commun 1989, V7, P97 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:241285 HCAPLUS

DOCUMENT NUMBER: 132:276307

TITLE: Methods and materials for detection and measurement of  
**free radical damage**

INVENTOR(S): Bar-Or, David; Lau, Edward

PATENT ASSIGNEE(S): Diagnostic Markers, Inc., USA

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020454	A1	20000413	WO 1999-US22746	19991001
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9962793	A1	20000426	AU 1999-62793	19991001
EP 1117686	A1	20010725	EP 1999-950055	19991001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.:

US 1998-102962 P 19981002

US 1998-165961 A 19981002

WO 1999-US22746 W 19991001

AB The present invention teaches a marker useful for detection and measurement of free radical damage. Specifically, the invention takes advantage of alterations which occur to the N-terminus of the albumin mol., a circulating protein in human blood, in the presence of free radicals. These alterations effect the ability of the N-terminus of the albumin mol. to bind metals. Methods for detecting and quantifying this alteration include evaluating and quantifying the cobalt binding capacity of an albumin-contg. sample, anal. and measurement of the ability of albumin to bind exogenous cobalt, detection and measurement of the presence of copper in a purified albumin sample and use of an immunol. assay specific to the altered form of serum albumin which occurs following free radical damage. Also taught by the present invention is the use of the peptide Asp Ala His Lys and the compd. Asp-Ala-His-Lys-R, wherein R is any chem. group capable of producing a detectable signal when a metal ion capable of binding to the N-terminus of naturally-occurring albumin is bound to the compd., for detection and quantitation of the marker. Methods of the present invention also include use of the marker as a "biochem. tag", thereby allowing for sensitive detection and measurement of the efficacy of clin. drugs and therapeutics which result in the generation of free radicals or which act to limit free radical damage. The marker also acts as a "biol. tag" of a process implicated in a wide array of diseases and conditions and, accordingly, may be used to monitor and assess such diseases and conditions. Finally, the invention provides antibodies, immunoassays, and kits for use in detecting or quantitating the marker.

IC ICM C07K014-47

ICS C07K016-06; G01N033-534  
 CC 9-16 (Biochemical Methods)  
 Section cross-reference(s): 1, 14  
 ST detection **free radical damage**  
 IT **Radicals**, biological studies  
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
 (damage; methods and materials for detection and measurement  
 of **free radical damage**)  
 IT Transition **metals**, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (ions; methods and materials for detection and measurement of  
**free radical damage**)  
 IT **Atomic absorption spectrometry**  
**Atomic emission spectrometry**  
 Containers  
 Disease, animal  
 Drugs  
**Immunoassay**  
 Test kits  
 Therapy  
 (methods and materials for detection and measurement of **free**  
**radical damage**)  
 IT **Antibodies**  
 RL: ANT (Analyte); ANST (Analytical study)  
 (methods and materials for detection and measurement of **free**  
**radical damage**)  
 IT **Albumins**, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (methods and materials for detection and measurement of **free**  
**radical damage**)  
 IT **Metals**, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (methods and materials for detection and measurement of **free**  
**radical damage**)  
 IT Peptides, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (methods and materials for detection and measurement of **free**  
**radical damage**)  
 IT Periodic system  
 (salt of transition **metal** ions; methods and materials for  
 detection and measurement of **free radical**  
**damage**)  
 IT **Albumins**, biological studies  
**Albumins**, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (serum; methods and materials for detection and measurement of  
**free radical damage**)  
 IT 7439-89-6D, Iron, salts 7439-92-1D, Lead, salts 7439-96-5D, Manganese,  
 salts 7439-97-6D, Mercury, salts 7439-98-7D, Molybdenum, salts  
 7440-02-0D, Nickel, salts 7440-22-4D, Silver, salts 7440-36-0D,  
 Antimony, salts 7440-38-2D, Arsenic, salts 7440-39-3D, Barium, salts  
 7440-43-9D, Cadmium, salts 7440-47-3D, Chromium, salts 7440-48-4,  
 Cobalt, biological studies 7440-48-4D, Cobalt, salts 7440-50-8D,  
 Copper, salts 7440-57-5D, Gold, salts 7440-62-2D, Vanadium, salts  
 7440-66-6D, Zinc, salts 111543-77-2, Asp-Ala-His-Lys  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (methods and materials for detection and measurement of **free**  
**radical damage**)  
 IT 134872-38-1 263698-69-7  
 RL: PRP (Properties)

(unclaimed sequence; methods and materials for detection and measurement of **free radical damage**)

REFERENCE COUNT: 3

REFERENCE(S): (1) Cotellet, N; Journal of Inorganic Biochemistry 1992, V46, P7 HCAPLUS  
(2) Keller, R; Chem Res Toxicol 1993, V6(4), P430 HCAPLUS  
(3) Laussac, J; Biochemistry 1984, V23(12), P2832 HCAPLUS

L25 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:94175 HCAPLUS

DOCUMENT NUMBER: 132:276022

TITLE: Increased oxidative modification of albumin when illuminated in vitro in the presence of a common sunscreen ingredient: protection by nitroxide radicals  
AUTHOR(S): Damiani, E.; Carloni, P.; Biondi, C.; Greci, L.  
CORPORATE SOURCE: Dipartimento di Scienze dei Materiali e della Terra, Università degli Studi di Ancona, Ancona, Italy  
SOURCE: Free Radical Biol. Med. (2000), 28(2), 193-201  
CODEN: FRBMEH; ISSN: 0891-5849

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We previously reported on the ability of dibenzoylmethane (DBM) and a relative, Parsol 1789, used as a UV A (UVA)-absorbing sunscreen, to generate free radicals upon illumination, and as a consequence, to inflict strand breaks in plasmid DNA in vitro. This study has now been extended to det. the effects of Parsol 1789 and DBM on proteins, under UVA illumination, with the sole purpose of gaining more knowledge on the photobiol. effects of sunscreen chems. Parsol 1789 (100 .mu.M) caused a 2-fold increase in protein carbonyl formation (an index of oxidative damage) in bovine serum albumin (BSA) when exposed to illumination, and this damage was both concn.- and time-dependent. The degree of protein damage was markedly reduced by the presence of free radical scavengers, namely piperidinic and indolinonic nitroxide radicals, in accordance with our previous study. Vitamin E had no effect under the conditions used. The results obtained corroborate the fact that Parsol 1789 generates free radicals upon illumination and that these are, most probably, responsible for the protein damage obsd. under the conditions used in our system. However, at present, we cannot extrapolate from these results the relevance to human use of sunscreens; therefore, further studies should be necessary to det. the efficacy at the mol. and cellular level of this UVA-absorber in order to ascertain protection against photocarcinogenic risk.

CC 8-9 (Radiation Biochemistry)

IT Carcinogens

(photo; sunscreen-induced **free radical** generation and serum **albumin damage** by UVA illumination and antioxidant action of nitroxide **radicals**)

IT **Albumins**, biological studies

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
(serum; sunscreen-induced **free radical** generation and serum **albumin damage** by UVA illumination and antioxidant action of nitroxide **radicals**)

IT Antioxidants

Oxidative stress, biological

Sunscreens

UV A radiation

(sunscreen-induced **free radical** generation and

- serum **albumin damage** by UVA illumination and  
antioxidant action of nitroxide **radicals**)
- IT Nitroxides  
RL: BAC (Biological activity or effector, except adverse); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(sunscreen-induced **free radical** generation and  
serum **albumin damage** by UVA illumination and  
antioxidant action of nitroxide **radicals**)
- IT **Radicals**, biological studies  
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
(sunscreen-induced **free radical** generation and  
serum **albumin damage** by UVA illumination and  
antioxidant action of nitroxide **radicals**)
- IT 120-46-7, Dibenzoylmethane 70356-09-1, Parsol 1789  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(sunscreen-induced **free radical** generation and  
serum **albumin damage** by UVA illumination and  
antioxidant action of nitroxide **radicals**)
- IT 1406-18-4, Vitamin e 2226-96-2, Tempol 2564-83-2, Tempo 57309-27-0  
57309-28-1 57309-32-7 57309-38-3  
RL: BAC (Biological activity or effector, except adverse); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(sunscreen-induced **free radical** generation and  
serum **albumin damage** by UVA illumination and  
antioxidant action of nitroxide **radicals**)
- IT 50-01-1, Guanidine hydrochloride 119-26-6, 2,4-Dinitrophenylhydrazine  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(sunscreen-induced **free radical** generation and  
serum **albumin damage** by UVA illumination and  
antioxidant action of nitroxide **radicals**)

REFERENCE COUNT: 10

- REFERENCE(S): (1) Andrae, I; J Photochem Photobiol 1997, V37, P147  
HCAPLUS  
(3) Beckwith, A; J Am Chem Soc 1992, V114, P4983  
HCAPLUS  
(5) Chetelat, A; Mutat Res 1993, V292, P241 HCAPLUS  
(8) Falcioni, G; Free Radic Res 1998, V28, P507  
HCAPLUS  
(9) Fuchs, J; Free Radic Biol Med 1998, V24, P643  
HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:600725 HCAPLUS

DOCUMENT NUMBER: 132:191265

TITLE: Development and application of novel biomarkers  
specific to **free radical** and lipid  
peroxidation modified proteins

AUTHOR(S): Osawa, Toshihiko

CORPORATE SOURCE: Nagoya University School of Bioagricultural Science,  
Nagoya, 464-8601, Japan

SOURCE: Furi Rajikaru no Rinsho (1998), 13, 8-13

CODEN: FRRIFI

PUBLISHER: Nihon Igakukan

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review with 23 refs. Lipid peroxidn. is known to be a free radical  
chain reaction which takes place in vivo and in vitro and forms lipid  
hydroperoxides and secondary products. These lipid peroxidn. products are  
highly reactive and have been shown to interact with many biol. components

such as proteins, amino acids, amines, and DNA. Recently we have been involved in developing a novel type of evaluation systems for oxidative stress using immunochem. methods by application of polyclonal antibodies which are specific to 13-hydroperoxy linoleic acid (13-HPODE), malondialdehyde (MDA) and 4-hydroxy-4-nonenal (HNE), because immuno-chem. methods are specific, simple and convenient. We have also succeeded in developing a novel monoclonal antibody which are specific to HNE-modified BSA. We made an evaluation by monitoring the amt. of 8-OH-dG in biol. samples using the monoclonal antibody method, and succeeded in developing a new ELISA method in quantitating 8-OH-dG by competitive inhibition. These immunochem. methods for detection of lipid peroxidn. products and oxidatively damaged DNA are very specific and useful technique to investigate the lipid peroxidn. mechanism from the view point of mol. level. By application of the immunochem. technique to the antioxidative assay systems, we can make the reliable, simple and convenient evaluation methods of antioxidative substances.

CC 9-0 (Biochemical Methods)

IT Antioxidants

**Immunoassay**

Oxidative stress, biological

(development and application of novel biomarkers specific to **free radical** and lipid peroxidn. modified proteins)

IT Proteins, general, biological studies

**Radicals**, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(development and application of novel biomarkers specific to **free radical** and lipid peroxidn. modified proteins)

IT **Immunoassay**

(enzyme-linked immunosorbent **assay**; development and application of novel biomarkers specific to **free radical** and lipid peroxidn. modified proteins)

IT Lipids, analysis

RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)

(hydroperoxides; development and application of novel biomarkers specific to **free radical** and lipid peroxidn. modified proteins)

IT Peroxidation

(lipid; development and application of novel biomarkers specific to **free radical** and lipid peroxidn. modified proteins)

IT Hydroperoxides

Peroxides, analysis

RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)

(lipid; development and application of novel biomarkers specific to **free radical** and lipid peroxidn. modified proteins)

IT Lipids, analysis

RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)

(peroxides; development and application of novel biomarkers specific to **free radical** and lipid peroxidn. modified proteins)

IT Lipids, analysis

RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)

(peroxidn.; development and application of novel biomarkers specific to **free radical** and lipid peroxidn. modified proteins)

IT **Albumins**, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(serum, bovine; development and application of novel biomarkers specific to **free radical** and lipid peroxidn.)



modified proteins)  
 IT 542-78-9, Malondialdehyde 23017-93-8 29343-52-0, 4-Hydroxy-2-nonenal  
 88847-89-6, 8-Hydroxy-2'-deoxy-guanosine  
 RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical  
 study); BIOL (Biological study)  
 (development and application of novel biomarkers specific to  
**free radical** and lipid peroxidn. modified proteins)

L25 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:558281 HCAPLUS  
 DOCUMENT NUMBER: 131:307072  
 TITLE: The Hydroxyl Free Radical Reactions of Ascorbyl  
 Palmitate as Measured in Various in Vitro Models  
 AUTHOR(S): Perricone, N.; Nagy, K.; Horvath, F.; Dajko, G.; Uray,  
 I.; Zs.-Nagy, I.  
 CORPORATE SOURCE: Department of Dermatology, Yale School of Medicine,  
 New Haven, CT, USA  
 SOURCE: Biochem. Biophys. Res. Commun. (1999), 262(3), 661-665  
 CODEN: BBRC9; ISSN: 0006-291X  
 PUBLISHER: Academic Press  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The OH.bul. free radical scavenging properties of ascorbyl palmitate (AP),  
 water-solubilized in the presence of a surfactant (Brij 35), were tested  
 in various systems: (1) The inhibition of polymn. of bovine serum albumin  
 by OH.bul. free radicals generated by the Fenton reaction indicated AP  
 exerts a considerable protective effect against polymn. by scavenging the  
 OH.bul. free radicals. (2) ESR spin trapping comparisons of DMPO with AP  
 were conducted. Using the Fenton reaction as a source of OH.bul. free  
 radicals, AP was 1 order of magnitude faster in scavenging these radicals  
 than DMPO. (3) Oxidative modification of BSA by 60Co-gamma irradiation of 80  
 krad, results in a strong increase in protein carbonyl content. AP  
 inhibits carbonyl formation very efficiently, indicating that AP may be  
 utilized as a biol. OH.bul. free radical scavenger in human therapy. (c)  
 1999 Academic Press.

CC 1-12 (Pharmacology)

IT Oxidation

(ascorbyl palmitate as **free radical** scavenger:  
 .gamma.-ray-induced oxidative **damage** of **albumin**)

IT Gamma ray

(irradiation; ascorbyl palmitate as **free radical**  
 scavenger: .gamma.-ray-induced oxidative **damage** of  
**albumin**)

REFERENCE COUNT: 32

REFERENCE(S): (1) Aiedeh, K; J Microencapsul 1997, V14, P567 HCAPLUS  
 (2) Baader, W; Biochem Pharmacol 1988, V37, P1089  
 HCAPLUS  
 (3) Battalora, M; Carcinogenesis 1993, V14, P2507  
 HCAPLUS  
 (4) Bissett, D; Photodermatol Photoimmunol Photomed  
 1990, V7, P56 HCAPLUS  
 (5) Bruun-Jensen, L; Z Lebensm Untersuch Forsch 1994,  
 V199, P210 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:200666 HCAPLUS  
 DOCUMENT NUMBER: 128:293113  
 TITLE: Chelating effect of human serum proteins on  
**metal-catalyzed ascorbate radical generation**

AUTHOR(S): Satoh, Kazue; Ida, Yoshiteru; Kimura, Satoshi;  
Taguchi, Kazumi; Numaguchi, Masahide; Gomi, Kunihide;  
Kochi, Mutsuyuki; Sakagami, Hiroshi

CORPORATE SOURCE: Analysis Center, School of Pharmaceutical Sciences,  
Showa University, Tokyo, 142, Japan

SOURCE: Anticancer Res. (1997), 17(6D), 4377-4380  
CODEN: ANTRD4; ISSN: 0250-7005

PUBLISHER: Anticancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Purified human serum albumin and IgG (IgG) were investigated for their  
metal-chelating activity, using ESR spectroscopy. Both copper (Cu<sup>2+</sup>) and  
iron ions (Fe<sup>3+</sup>) enhanced the radical intensity of both sodium ascorbate  
and sodium 5,6-benzylidene-L-ascorbate (SBA). Albumin significantly  
reduced the stimulation effect of copper, but not that of iron. On the  
other hand, IgG effectively reduced the radical intensity of iron, without  
affecting that of copper. The present study demonstrates the specific  
chelating action of these serum proteins, suggesting their possible  
preventive effects on metal-catalyzed pathogenic diseases.

CC 13-2 (Mammalian Biochemistry)

ST serum protein **metal** catalyzed ascorbate radical; iron copper  
chelation serum **albumin** IgG

IT Chelation  
(chelating effect of human serum proteins on **metal**-catalyzed  
ascorbate radical generation)

IT IgG  
Serum **albumin**  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological  
process); BIOL (Biological study); PROC (Process)  
(chelating effect of human serum proteins on **metal**-catalyzed  
ascorbate radical generation)

IT 7439-89-6, Iron, biological studies 7440-50-8, Copper, biological  
studies  
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
(chelating effect of human serum proteins on **metal**-catalyzed  
ascorbate radical generation)

IT 6730-29-6, L-Ascorbic acid, **free radical** from  
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation,  
nonpreparative)  
(chelating effect of human serum proteins on **metal**-catalyzed  
ascorbate **radical** generation)

L25 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1994:646338 HCAPLUS

DOCUMENT NUMBER: 121:246338

TITLE: Superoxide dismutase gene mutations as causes of  
neurodegenerative diseases and compounds and methods  
for the diagnosis, treatment, and prevention of the  
diseases

INVENTOR(S): Brown, Robert; Horvitz, H. Robert; Rosen, Daniel R.

PATENT ASSIGNEE(S): General Hospital Corp., USA; Massachusetts Institute  
of Technology

SOURCE: PCT Int. Appl., 98 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.

KIND DATE

APPLICATION NO. DATE

WO 9419493	A1	19940901	WO 1994-US2089	19940228
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5843641	A	19981201	US 1993-23980	19930226
CA 2157041	AA	19940901	CA 1994-2157041	19940228
EP 686203	A1	19951213	EP 1994-910183	19940228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08510377	T2	19961105	JP 1994-519309	19940228
US 5849290	A	19981215	US 1995-486953	19950607
PRIORITY APPLN. INFO.:			US 1993-23980	19930226
			US 1994-204052	19940228
			WO 1994-US2089	19940228

AB Disclosed is the family of genes responsible for the neurodegenerative diseases, particularly amyotrophic lateral sclerosis (ALS). Methods and compds. for the diagnosis, prevention, and therapy of the disease are also disclosed. Uses of the compds. in the prepn. of diagnostic and therapeutic medicaments are also provided. Fourteen different SOD1 missense mutations in 16 different familial ALS families were identified. The mutations were identified by PCR followed by single-strand conformational polymorphism anal. The most common single mutation was an Ala-4 to Val substitution in exon 1. This mutation reduced the total SOD activity by 50% compared to normal controls. Addnl. polymorphisms were identified in exons 3 and 4 as well as in intron 3. Some of these mutations are detectable by restriction fragment length polymorphism.

IC ICM C12Q001-68  
ICS C12P019-34; C07H021-04  
CC 1-11 (Pharmacology)  
Section cross-reference(s): 3, 9, 14

IT **Antibodies**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(anti-SOD; superoxide dismutase gene mutations as causes of neurodegenerative diseases and compds. and methods for diagnosis, treatment, and prevention of the diseases)

IT **Enzymes**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(free radical-producing, inhibitors of; superoxide dismutase gene mutations as causes of neurodegenerative diseases and compds. and methods for diagnosis, treatment, and prevention of the diseases)

IT **Albumins, biological studies**

Ferritins  
Lazaroids

**Metallothioneins**

Sulfonamides  
Thiols, biological studies  
Transferrins

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(superoxide dismutase gene mutations as causes of neurodegenerative diseases and compds. and methods for diagnosis, treatment, and prevention of the diseases)

IT **Proteins, specific or class**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(metal-binding, apo-; superoxide dismutase gene mutations as causes of neurodegenerative diseases and compds. and methods for diagnosis, treatment, and prevention of the diseases)

IT **Antibodies**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(monoclonal, anti-SOD; superoxide dismutase gene mutations as causes of neurodegenerative diseases and compds. and methods for diagnosis,

treatment, and prevention of the diseases)

L25 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1994:418077 HCAPLUS

DOCUMENT NUMBER: 121:18077

TITLE: Radiopharmaceutical bacteriostats comprising benzalkonium and benzethorium chloride

INVENTOR(S): Tartaglia, Daniel; Flanagan, Richard J.

PATENT ASSIGNEE(S): Merck Frosst Canada, Inc., Can.

SOURCE: U.S., 18 pp. Cont.-in-part of U.S. 5,227,152.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5306482	A	19940426	US 1992-841281	19920303
US 5093105	A	19920303	US 1991-682170	19910409
US 5227152	A	19930713	US 1991-806572	19911212
CA 2065462	AA	19921010	CA 1992-2065462	19920407
EP 508724	A1	19921014	EP 1992-303074	19920407
EP 508724	B1	19960807		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE				
AT 141059	E	19960815	AT 1992-303074	19920407
JP 05271102	A2	19931019	JP 1992-133069	19920409
JP 07072144	B4	19950802		

PRIORITY APPLN. INFO.:

US 1991-682170	19910409
US 1991-806572	19911212
US 1992-841281	19920303

AB Benzalkonium chloride (I) and benzethorium chloride are useful in radiopharmaceutical preps. (optionally in the presence of a polymyxin or a polymyxin deriv.) as bacteriostatic agents which are compatible with anti-oxidants. A compn. contg. methylene diphosphonic acid 10, SnCl<sub>2</sub>.2H<sub>2</sub>O 1, PABA 2 mg, and I 50.mu.g was prepd. and lyophilized. The compn. was reconstituted with 500mCi 99Tc Na pertechnetate in 10mL water and left at room temp. for 24 h. The amt. of TcO<sub>4</sub> in the soln. after this period was <1%.

IC ICM A61K043-00

ICS A61K049-02

NCL 424001370

CC 63-6 (Pharmaceuticals)

IT **Radicals**, biological studies

RL: BIOL (Biological study)

(free, scavengers of, radiopharmaceuticals contg. bacteriostats and)

IT **Antibodies**

RL: BIOL (Biological study)

(monoclonal, to fibrin and myosin, complexes with technetium 99-m, radiopharmaceuticals contg. benzalkonium and benzethorium chloride bacteriostats and)

IT **Albumins**, uses

RL: BIOL (Biological study)

(technetium complexes, labeled with technetium-99, radiopharmaceuticals contg. benzalkonium and benzethorium chloride bacteriostats and)

IT 14133-76-7DP, Technetium 99, complexes with **albumins**, preparation

RL: PREP (Preparation)

(metastable, radiopharmaceuticals contg. benzalkonium and benzethorium

chloride bacteriostats and)

L25 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1993:211487 HCAPLUS

DOCUMENT NUMBER: 118:211487

TITLE: A fluorescamine-based **assay** for the degree of glycation in bovine serum **albumin**

AUTHOR(S): Yaylayan, Varoujan A.; Huyghues-Despointes, Alexis; Polydorides, Angeliki

CORPORATE SOURCE: Dep. Food Sci. Agric. Chem., McGill Univ., Ste Anne de Bellevue, PQ, H9X 1C0, Can.

SOURCE: Food Res. Int. (1992), 25(4), 269-75

CODEN: FORIEU; ISSN: 0963-9969

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The fluorescence resulting from the reaction of a protein with fluorescamine is an indication of the no. of free amino groups in that protein, consequently glycated proteins which have fewer free amino groups will show less fluorescence. With the appropriate stds., the difference in fluorescence of glycated and non-glycated proteins can be translated into the no. of glycated sites in a protein. Glucose (0.22 M final concn.) was incubated with bovine serum albumin (BSA) (0.1 mg/mL) in a total vol. of 50 mL of 0.1 M phosphate buffer pH 7.2 at 37.degree. for a period of 35 days. To assess the effect of metal catalyzed free radical damage to the protein, the incubation was also carried out in the presence of a metal chelating agent EGTA (0.38 mg/mL). As expected, the fluorescence of both mixts. decreased with time, as more lysyl groups became glycated. Calcns. based on the std. curve of t-BOC-lysine showed that approx. 18 mol of glucose were incorporated per mol of BSA during the incubation in the presence of EGTA and 23 mol in the absence of EGTA. This difference is explained by the metal-catalyzed free radical fragmentation of BSA which exposes more N-terminal amino groups for reaction with glucose.

CC 17-1 (Food and Feed Chemistry)

ST **albumin** glycation assessment fluorescamine fluorescenceIT **Albumins**, analysis

RL: ANST (Analytical study)

(bovine, **assay** of degree of glycation of, fluorescamine fluorescence in)

IT Radical ions

(metal catalyzed formation of, bovine serum **albumin** fragmentation by, degree of glycation estn. from fluorescamine fluorescence in relation to)

IT Glycosidation

(glycation, of bovine serum **albumin**, fluorescamine fluorescence for **assay** for degree of)

IT Trace elements, miscellaneous

RL: MSC (Miscellaneous)

(metals, protein **free radical**damage catalyzed by, degree of glycation **assay** from fluorescamine fluorescence in relation to)

IT 38183-12-9, Fluorescamine

RL: ANST (Analytical study)

(bovine serum **albumin** interaction with, fluorescence from, degree of glycation estn. from)

L25 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1992:545016 HCAPLUS

DOCUMENT NUMBER: 117:145016

TITLE: Changes in **free radicals**, trace

elements, and neurophysiological function in rats with liver **damage** induced by D-galactosamine

AUTHOR(S): Hu, Henglong; Chen, Rendun

CORPORATE SOURCE: Dep. Nutr., Inst. Infect. Dis., Beijing, 100039, Peop. Rep. China

SOURCE: Biol. Trace Elem. Res. (1992), 34(1), 19-25  
CODEN: BTERDG; ISSN: 0163-4984

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The changes in trace elements, free radicals, and neurophysiol. function were investigated in rats with liver damage induced by D-galactosamine (GalN). The elevated results showed that all the parameters related to free radical metab. changed after administration of GalN. Relative free radical concn., malonaldehyde (MDA), and GSSG elevated, but GSH decreased. Concurrently, zinc, copper, manganese, and selenium contents in liver were significantly reduced, whereas iron was elevated. In rats with hepatic encephalopathy (HE) owing to fulminant hepatic failure (FHF) induced by a high dosage of GalN, the latencies of visual evoked potentials (VEPs) were delayed. Moreover, there is a correlation between Zn content of brain and the latencies of VEPs. The results of this study suggested that lipid peroxidn. by free radicals might be responsible for GalN-induced liver damage in which trace elements were involved, and that change in brain Zn might play a role in the neural inhibition of HE owing to FHF.

CC 4-3 (Toxicology)

IT Liver, toxic chemical and physical **damage**  
(galactosamine toxicity to, **free radicals** and trace elements and neurophysiol. during)

IT **Albumins**, biological studies  
Prealbumins

RL: BIOL (Biological study)  
(of tissue, galactosamine effect on, other tissues comparison with, hepatotoxicity in relation to)

IT Trace elements, biological studies

RL: BIOL (Biological study)  
(heavy **metals**, in galactosamine toxicity to liver)

IT 7535-00-4, D-Galactosamine

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(toxicity of, to liver, **free radicals** and trace elements and neurophysiol. during)

L25 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1992:35817 HCAPLUS

DOCUMENT NUMBER: 116:35817

TITLE: **Radical-induced damage** to  
proteins: ESR spin-trapping studies

AUTHOR(S): Davies, Michael J.; Gilbert, Bruce C.; Haywood, Rachel M.

CORPORATE SOURCE: Dep. Chem., Univ. York, Heslington/York, YO1 5DD, UK

SOURCE: Free Radical Res. Commun. (1991), 15(2), 111-27

CODEN: FRRCEX; ISSN: 8755-0199

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The reactions of hydroxyl radicals generated from FeII/H2O2 and CuII/H2O2 redox couples with a variety of proteins (bovine serum albumin, histones, cytochrome c, lysozyme and protamine) are investigated by ESR spin trapping. The signals obtained, which are generally anisotropic in nature, characterize the formation of partially immobilized spin-adducts resulting from attack of the HO.bul. radicals on the protein and subsequent reaction of the protein-derived radicals with the spin trap. Similar spin adducts are obsd. on incubation of two heme-proteins (Hb and

myoglobin) with H<sub>2</sub>O<sub>2</sub> in the absence of added metal ions implying a reaction at the heme center followed by internal electron transfer reactions. Two strategies are employed to obtain information about the site(s) of radical damage in these proteins. The first involves the use of a variety of spin traps and in particular DMPO: with this particular trap the broad spectra from largely immobilized radicals show characteristic  $\alpha$  ( $\beta$ -H) values which enable carbon-, oxygen- and sulfur-centered radicals to be distinguished. The second involves the use of enzymic cleavage of first-formed adducts to release smaller nitroxides, with isotropic spectra, which allow the recognition of  $\beta$ -proton splittings and hence information about the sites of radical damage to be obtained. These results, which allows backbone and side-chain attack to be distinguished, are in agreement with random attack of the HO $\cdot$  radical on the protein and are in accord with studies carried out on model peptides. In contrast the use of less reactive attacking radicals [N<sub>3</sub> $\cdot$ ,  $\cdot$ CH(CH<sub>3</sub>)OH] and oxidizing agents (Ce<sup>4+</sup>) provides evidence for selective attack on these proteins at particular residues.

- CC 4-3 (Toxicology)  
Section cross-reference(s): 6
- ST **radical protein damage**; hydroxyl **radical**  
protein **damage**; hydrogen peroxide **metal** protein oxidn;  
oxidative **damage radical** protein
- IT Histones  
RL: BIOL (Biological study)  
(2S, hydroxyl **radical**-induced **damage** of, after  
reaction with hydrogen peroxide and **metal**, ESR in studies of)
- IT Oxidative stress, biological  
(hydrogen peroxide and **metal** mediation of, protein damage  
induction by, ESR in studies of)
- IT **Albumins**, biological studies  
Hemoglobins, met-  
Myoglobins  
Protamines  
RL: BIOL (Biological study)  
(hydroxyl **radical**-induced **damage** of, after reaction  
with hydrogen peroxide and **metal**, ESR in studies of)
- IT **Radicals**, biological studies  
RL: BIOL (Biological study)  
(protein **damage** induction by, ESR in studies of)
- IT Proteins, biological studies  
RL: BIOL (Biological study)  
(**radical**-induced **damage** of, ESR in studies of)
- IT Histones  
RL: BIOL (Biological study)  
(H<sub>2</sub>A, hydroxyl **radical**-induced **damage** of, after  
reaction with hydrogen peroxide and **metal**, ESR in studies of)
- IT 3695-73-6 5874-90-8 7093-67-6 17123-30-7 19729-30-7 24991-23-9  
25513-46-6, Polyglutamic acid 25608-40-6, Polyaspartic acid  
26063-13-8, Polyaspartic acid 26894-34-8, Polyasparagine 28088-48-4,  
Polyasparagine 70195-20-9  
RL: BIOL (Biological study)  
(hydroxyl **radical** reaction with, ESR in studies of,  
**radical**-induced **damage** of proteins in relation to)
- IT 56-86-0, L-Glutamic acid, properties 56-87-1, L-Lysine, properties  
59-51-8, DL-Methionine 63-91-2, L-Phenylalanine, properties 73-22-3,  
L-Tryptophan, properties 74-79-3, L-Arginine, properties 302-72-7,  
DL-Alanine 328-39-2, DL-Leucine 556-33-2 556-50-3 637-84-3  
687-69-4 837-83-2 926-79-4  
RL: PRP (Properties)  
(hydroxyl **radical** reaction with, ESR in studies of,

- IT 9001-63-2, Lysozyme 9007-43-6, Cytochrome c, biological studies  
 RL: BIOL (Biological study)  
 (hydroxyl **radical**-induced **damage** of, after reaction  
 with hydrogen peroxide and **metal**, ESR in studies of)
- IT 2348-46-1 12596-60-0, biological studies  
 RL: BIOL (Biological study)  
 (lysozyme **damage** induction by, **radical**-induced  
**damage** of proteins in relation to)
- IT 7440-50-8, Copper, biological studies 15651-72-6  
 RL: BIOL (Biological study)  
 (protein **damage** induction by hydrogen peroxide and, hydroxyl  
**radical** mediation of, ESR in studies of)
- IT 7722-84-1, Hydrogen peroxide (H2O2), biological studies  
 RL: BIOL (Biological study)  
 (protein **damage** induction by iron and copper and, hydroxyl  
**radical** mediation of, ESR in studies of)
- IT 3352-57-6, Hydroxyl **radical**, biological studies  
 RL: BIOL (Biological study)  
 (protein **damage** induction by, ESR in studies of)
- IT 7440-45-1, Cerium, reactions  
 RL: RCT (Reactant)  
 (reaction of, with **albumin**, ESR in studies of,  
**radical**-induced **damage** of proteins in relation to)

L25 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1992:1867 HCAPLUS

DOCUMENT NUMBER: 116:1867

TITLE: Free radical damage to proteins: the influence of the  
 relative localization of radical generation,  
 antioxidants, and target proteins

AUTHOR(S): Dean, Roger T.; Hunt, James V.; Grant, Adrienne J.;  
 Yamamoto, Yorihiro; Niki, Etsuo

CORPORATE SOURCE: Heart Res. Inst., Sydney, 2050, Australia

SOURCE: Free Radical Biol. Med. (1991), 11(2), 161-78  
 CODEN: FRBMEH; ISSN: 0891-5849

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Free radicals were generated at known rates in the aq. phase (by means of  
 2,2'-azobis (2-amidinopropane) dihydrochloride [AAPH]) and a membranous  
 (lipid) phase (by means of 2,2'-azobis (2,4-dimethylvaleronitrile [AMVN])).  
 A sol. protein (bovine serum albumin: BSA), and membranes of lysed  
 mitochondria contg. radioactively labeled monoamine oxidase (MAO), were  
 exposed to the resultant radical fluxes. Antioxidants were added to the  
 system, either in the aq. phase (Trolox) or in a liposomal membrane phase  
 (.alpha.-tocopherol). Protein damage was assessed as tryptophan oxidn.  
 and conformational changes in tryptophan fluorescence of the sol. protein  
 BSA, and as fragmentation of both BSA and monoamine oxidase. Radicals  
 generated in the aq. phase, by AAPH, were effective in damaging BSA and  
 MAO. Radicals generated within the liposome membrane phase (by AMVN) were  
 less effective against BSA than those deriving from AAPH. Liposomal AMVN  
 radicals could damage MAO, present in a sep. membranous phase, though  
 again, less effectively than could AAPH-derived radicals. BSA could be  
 protected by Trolox, the aq. sol. antioxidant, but hardly by tocopherol  
 itself. Damage to MAO was limited by Trolox, and also by the hydrophobic  
 antioxidant, tocopherol. Damaging reactions due to radicals generated in  
 a membrane phase were significantly accelerated when the membrane was  
 peroxidizable (soybean phosphatidylcholine) rather than nonperoxidizable  
 (satd. dimyristoyl phosphatidylcholine). Thus, lipid radicals also played  
 some role in protein damage in these systems. BSA was attacked similarly



in the presence or absence of liposomes by AAPH. Correspondingly, BSA could inhibit the peroxidn. of liposomes induced by AAPH and less efficiently that induced by AMVN. Evidently, the relative localization of radical generation, antioxidants, and protein targets has a major influence on the extent of radical attack on proteins and membranes.

CC 4-3 (Toxicology)

IT **Albumins**, biological studies

RL: BIOL (Biological study)  
(**free radical damage** of)

L25 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1991:527570 HCAPLUS

DOCUMENT NUMBER: 115:127570

TITLE: **Free radical**-induced carbonyl content in protein of estrogen-treated hamsters **assayed** by sodium boro[3H]hydride reduction

AUTHOR(S): Winter, Mark L.; Liehr, Joachim G.

CORPORATE SOURCE: Dep. Pharmacol. Toxicol., Univ. Texas, Galveston, TX, 77550-2774, USA

SOURCE: J. Biol. Chem. (1991), 266(22), 14446-50

CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Oxidn. damage to proteins is known to occur via conversion of side chain amino groups to corresponding carbonyl derivs. Such damage to enzymes and purified proteins has been quantified previously by redn. with sodium boro[3H]hydride and subsequent measurement of the incorporation of 3H into amino acid fractions. In this study, the NaB3H4 redn. assay was modified to permit the quantitation of free radical-mediated oxidative damage to proteins obtained from animals. Modifications included addnl. extns. of protein isolates with org. solvents to remove lipids and with nitric acid to remove metal ions. The modified assay has first been validated in vitro by measuring changes in levels of oxidative damage to bovine serum albumin exposed to xanthine plus xanthine oxidase (2-fold increase), to hydrogen peroxide and iron(II) sulfate (5-fold increase), or to .gamma. radiation (30-fold increase over controls, resp.). .gamma. Radiation of isolated hamster kidney protein also raised the carbonyl content in a dose-dependent manner. The modified assay has been validated in vivo by measuring the changes in oxidative damage to lung tissue in animals exposed to .apprx.85% oxygen (2-fold increase) or to different doses of paraquat (5-fold increases with the high dose over controls, resp.). The assay was then used to examine free radical-mediated oxidn. introduced by acute or chronic treatment of hamsters with estrogens, since both synthetic and natural estrogens induce kidney tumors in this species. Priming of hamsters for 3 days with 20 mg/kg/day diethylstilbestrol and treatment with 100 mg/kg of this drug on the 4th day resulted in a 160% increase in free radical modification of renal proteins. Oxidative damage to kidney proteins was also assayed in hamsters treated with estradiol implants for <7 mo, a regimen known to induce kidney tumors. Significant increases in covalent oxidative modification to renal proteins over values in age-matched controls were detected after 1, 2, and 7 mo of continuous estradiol exposure. Thus, the modification of the NaB3H4 redn. assay is a useful postlabeling method for monitoring free radical action in vivo. Furthermore, it is postulated that free radical damage in estrogen-treated hamster kidney plays a role in estrogen-induced carcinogenesis.

CC 2-4 (Mammalian Hormones)

Section cross-reference(s): 4, 8, 9, 14

ST estrogen protein **damage** kidney carcinogenesis; **free radical** carbonyl protein **damage**; sodium borohydride protein **damage** detn

- IT Proteins, biological studies  
RL: BIOL (Biological study)  
(estrogen-induced damage of, of kidney, carbonyl detn. by borohydride redn. in **assay** of)
- IT Kidney, toxic chemical and physical damage  
(from estrogens, preradicals in, carbonyl detn. in protein by borohydride redn. in **assay** of)
- IT Lung, toxic chemical and physical damage  
(from hyperoxia and paraquat, carbonyl detn. in protein by borohydride redn. **assay** of)
- IT **Radicals**, biological studies  
RL: BIOL (Biological study)  
(in estrogen-induced kidney oxidative **damage**)
- IT Gamma ray, biological effects  
(kidney protein oxidative damage from, carbonyl detn. by borohydride redn. in **assay** of)
- IT Hyperoxia  
(long oxidative damage from, protein carbonyl detn. by borohydride redn. in **assay** of)
- IT 7720-78-7, Iron(II) sulfate  
RL: BIOL (Biological study)  
(**albumin** oxidative damage from hydrogen peroxide and, carbonyl detn. by borohydride redn. in **assay** of)
- IT 7722-84-1, Hydrogen peroxide, biological studies  
RL: BIOL (Biological study)  
(**albumin** oxidative damage from iron sulfate and, carbonyl detn. by borohydrate redn. in **assay** of)
- IT 9002-17-9, Xanthine oxidase  
RL: BIOL (Biological study)  
(**albumin** oxidative damage from xanthine and, carbonyl content detn. by borohydride redn. in **assay** of)
- IT 69-89-6, Xanthine  
RL: BIOL (Biological study)  
(**albumin** oxidative damage from xanthine oxidase and, carbonyl content detn. by borohydrate redn. in **assay** of)
- IT 4685-14-7, Paraquat  
RL: BIOL (Biological study)  
(long oxidative damage from, protein carbonyl detn. by borohydride redn. in **assay** of)

L25 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1991:422201 HCAPLUS

DOCUMENT NUMBER: 115:22201

TITLE: Superoxide dismutase-catalase conjugates as tissue-specific therapeutics

INVENTOR(S): Poznansky, Mark J.; Mao, Guo Dong

PATENT ASSIGNEE(S): University of Alberta, Can.

SOURCE: PCT Int. Appl., 30 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9103548	A1	19910321	WO 1990-CA279	19900830
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
CA 2065430	AA	19910301	CA 1990-2065430	19900830

AU 9062854	A1	19910408	AU 1990-62854	19900830
US 5336493	A	19940809	US 1992-836274	19920302
PRIORITY APPLN. INFO.:			GB 1989-19661	19890831
			WO 1990-CA279	19900830

AB A novel multicomponent conjugate having superoxide dismutase (SOD), catalase, and optionally albumin and a targeting agent such as antibody is provided. A pharmaceutical compn. contg. such conjugate can be used for tissue-specific scavenging of superoxide and hydroxyl radicals with higher efficiency than SOD or catalase alone. The half-life of the SOD-catalase conjugates was 300 min in rats. Scavenging of the free radicals using the conjugates was also demonstrated in vitro and in the rat heart model of ischemia-reperfusion.

IC ICM C12N009-96

CC 1-4 (Pharmacology)

IT **Antibodies**

RL: BIOL (Biological study)  
(conjugates with superoxide dismutase and catalase, for tissue-specific scavenging of superoxide and hydroxyl **free radicals**)

IT **Myosins**

RL: BIOL (Biological study)  
(monoclonal **antibody** to, conjugates with superoxide dismutase and catalase, for tissue-specific scavenging of superoxide and hydroxyl radicals)

IT **Albumins, compounds**

RL: BIOL (Biological study)  
(conjugates, with superoxide dismutase and catalase, for tissue-specific scavenging of superoxide and hydroxyl radicals)

IT **Antibodies**

RL: BIOL (Biological study)  
(monoclonal, conjugates with superoxide dismutase and catalase, for tissue-specific scavenging of superoxide and hydroxyl **free radicals**)

IT 9001-05-2DP, Catalase, conjugates with superoxide dismutase 9054-89-1DP, Superoxide dismutase, conjugates with catalase

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, for superoxide and hydroxyl **free radical** scavenging)

L25 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1991:201358 HCAPLUS

DOCUMENT NUMBER: 114:201358

TITLE: Stimulatory and inhibitory actions of proteins and amino acids on copper-catalyzed **free radical** generation in the bulk phase

AUTHOR(S): Simpson, Jeremy A.; Dean, Roger T.

CORPORATE SOURCE: Heart Res. Inst., Sydney, 2050, Australia

SOURCE: Free Radical Res. Commun. (1990), 10(4-5), 303-12

CODEN: FRRCEX; ISSN: 8755-0199

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effect of a variety of proteins and amino acids was investigated on oxygen free radical activity as assessed by copper/hydrogen peroxide induced benzoate hydroxylation as well as copper-catalyzed ascorbate autoxidn. Serum albumins from a variety of species (human, bovine, and dog) had both inhibitory and stimulatory effects depending on the molar copper to protein ratio; low ratios were inhibitory and high stimulatory. Some other proteins tested (lysozyme, soybean trypsin inhibitor, and conalbumin) also had dual (inhibitory and stimulatory) effects, as did both histidine and polyhistidine, but all effects occurred at different

molar ratios presumably dependent on the relative affinities for the copper ions. In contrast, metallothionein and ceruloplasmin, proteins specialized to bind copper in vivo, had no stimulatory effects. In addn. to their fairly well documented inhibitory effects, under certain conditions some proteins also stimulate radical reactions. The possible role of this phenomenon in vivo is discussed.

CC 4-3 (Toxicology)

ST protein amino acid copper **free radical**

IT **Albumins**, biological studies

Amino acids, biological studies

**Metallothioneins**

Proteins, biological studies

RL: BIOL (Biological study)

(copper-catalyzed **free radical** generation response to)

IT 71-00-1, Histidine, biological studies 1391-06-6, Conalbumin

9001-63-2, Lysozyme 9031-37-2, Ceruloplasmin 9078-38-0 26062-48-6,

Polyhistidine 26854-81-9, Polyhistidine

RL: BIOL (Biological study)

(copper-catalyzed **free radical** generation response to)

IT 7440-50-8, Copper, biological studies

RL: BIOL (Biological study)

(**free radical** generation catalyzed by, proteins and amino acids effect on)

L25 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1991:141132 HCAPLUS

DOCUMENT NUMBER: 114:141132

TITLE: Characterization of a monoclonal **antibody** to thymidine glycol monophosphate

AUTHOR(S): Chen, Bi Xing; Hubbard, Karen; Ide, Hiroshi; Wallace, Susan S.; Erlanger, Bernard F.

CORPORATE SOURCE: Coll. Physicians Surg., Columbia Univ., New York, NY, 10032, USA

SOURCE: Radiat. Res. (1990), 124(2), 131-6

CODEN: RAREAE; ISSN: 0033-7587

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A monoclonal antibody specific for thymine glycol (TG) in irradiated or OsO4-treated DNA was obtained by immunizing with thymidine glycol monophosphate (TMP-glycol) conjugated to bovine serum albumin by a carbodiimide procedure. Screening by dot-immunobinding and ELISA procedures gave 9 clones that bound OsO4-treated DNA. One of them, 2.6F.6B.6C, an IgG2a.kappa., was characterized further. Hapten inhibition studies with OsO4-treated DNA showed that the antibody was specific for TMP-glycol. Among the various inhibitors tested, inhibition was in the order TMP-glycol > 5,6-dihydrothymidine phosphate > TMP > thymidine glycol > TG. Inhibition by 5,6-dihydrothymidine, thymidine, thymine, AMP, and CMP was negligible. In OsO4-treated DNA, as few as 0.5 TG per 10,000 bp were detectable by direct ELISA. Inhibition assays could detect as few as 1.5 TG per 10,000 bp. The antibody was equally reactive with native or denatured DNA contg. TG. Among the X-irradiated homopolymers dC, dA, dG, and dT, only dT reacted with the antibody. Using an ELISA, the antibody could detect damage in irradiated DNA at the level of 20 Gy. Thus the antibody is of potential use in assays for DNA damage caused by X rays or other agents that damage DNA by free radical interactions.

CC 15-3 (Immunochemistry)

Section cross-reference(s): 8

ST monoclonal **antibody** thymidine glycol monophosphate

- IT Deoxyribonucleic acids  
RL: BIOL (Biological study)  
(**damage** to, from X-ray or **free radicals**,  
monoclonal **antibody** to thymidine glycol monophosphate in  
relation to)
- IT **Albumins**, compounds  
RL: PREP (Preparation)  
(conjugates, with thymidine glycol monophosphate, monoclonal  
**antibody** to, prepn. and characterization of)
- IT **Antibodies**  
RL: PREP (Preparation)  
(monoclonal, to thymidine glycol monophosphate, prepn. and  
characterization of)
- IT 365-07-1, Thymidine monophosphate 2943-56-8, Thymine glycol  
32645-65-1, Thymidine glycol 69321-99-9  
RL: BIOL (Biological study)  
(**antibody** to thymidine glycol monophosphate cross-reactivity  
with)
- IT 25086-81-1  
RL: BIOL (Biological study)  
(**antibody** to thymidine glycol monophosphate cross-reactivity  
with irradiated)
- IT 6168-31-6D, **albumin** conjugates  
RL: BIOL (Biological study)  
(monoclonal **antibody** to, prepn. and characterization of)

L25 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1991:94805 HCAPLUS  
DOCUMENT NUMBER: 114:94805  
TITLE: Antiinflammatory reactivity of copper(I)-thionein  
AUTHOR(S): Miesel, Ralf; Hartmann, Hans Juergen; Weser, Ulrich  
CORPORATE SOURCE: Physiol.-Chem. Inst., Univ. Tuebingen, Tuebingen,  
7400, Fed. Rep. Ger.  
SOURCE: Inflammation (N. Y.) (1990), 14(5), 471-83  
CODEN: INFLD4; ISSN: 0360-3997  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB In unseparated human blood the reactivity of yeast copper (I)-thionein on TPA-activated polymorphonuclear leukocytes was evaluated and compared with low-mol.-wt. Cu chelates exerting Cu, Zn-activated superoxide dismutase mimetic activity. Cu, 18 .mu.M, in the form of Cu-thionein was sufficient to inhibit the superoxide prodn. of activated human blood phagocytes by 50%. Furthermore, the scavenging of hydroxyl radicals and singlet oxygen by Cu(I)-thionein was detd., using the 2-deoxyribose fragmentation assay induced by decaying K3CrO8 and the NADPH oxidn. caused by UVA illuminated psoralen, resp. The inhibitory reactivity of Cu-thionein in both assays was compared with that of serum proteins including albumin, ceruloplasmin, transferrin, and ferritin. The galactosamine/endotoxin-induced hepatitis in male NMRI mice was used to evaluate the antiinflammatory reactivity of Cu-thionein in vivo. The serum Cu, superoxide dismutase, and sorbitol dehydrogenase concns., as well as the activity of polymorphonuclear leukocytes in unseparated blood seemed most appropriate to quantify the protective capacity of Cu-thionein in the course of an oxidative stress-dependent liver injury. The i.p. application of 32.5 .mu.mol/kg thionein-Cu limited this damage to 45%.

CC 1-7 (Pharmacology)

IT Phagocyte  
(oxygen **free radicals** formation by human, copper  
thionein inhibition of, anti-inflammatory mechanism in relation to)

IT **Albumins**, biological studies

Ferritins  
Transferrins  
RL: BIOL (Biological study)  
(scavenging of oxygen radicals in human phagocyte by copper thionein vs.)

IT **Metallothioneins**  
RL: PRP (Properties)  
(copper-contg., anti-inflammatory mechanism of)

IT Leukocyte  
(polymorphonuclear, oxygen **free radicals** formation by human, copper thionein inhibition of, anti-inflammatory mechanism in relation to)

L25 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1989:167750 HCAPLUS

DOCUMENT NUMBER: 110:167750

TITLE: Phycoerythrin fluorescence-based **assay** for peroxy radicals: a screen for biologically relevant protective agents

AUTHOR(S): DeLange, Robert J.; Glazer, Alexander N.

CORPORATE SOURCE: Dep. Microbiol. Immunol., Univ. California, Berkeley, CA, 94720, USA

SOURCE: Anal. Biochem. (1989), 177(2), 300-6

CODEN: ANBCA2; ISSN: 0003-2697

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Under the conditions of this assay, antioxidants that react rapidly with peroxy free radicals (e.g., ascorbate, vitamin E analogs, and urate), protect phycoerythrin completely from damage by such radicals generated by thermal decompn. of 2,2'-azobis[(2-amidinopropane)]; other compds. provide partial concn.-dependent protection. Change in phycoerythrin fluorescence emission with time provides a measure of the rate of free radical damage. The assay exploits the unusual reactivity of phycoerythrin toward these peroxy radicals. On a molar basis, phycoerythrin reacts with these radicals >100-fold slower than do ascorbate or vitamin E analogs, but >60-fold faster than other proteins. Applications of this assay to the estn. of the peroxy radical scavenging capacity of human plasma are described, and to the comparison of the scavenging properties of several proteins and of DNA, of vitamins and their derivs., of catecholamine neurotransmitters, and of a variety of other low-mol.-wt. biol. compds.

CC 4-3 (Toxicology)

IT Blood plasma  
(oxygen **radical damage** to phycoerythrin in, of humans, protective agent screening in relation to)

IT Antioxidants  
Vitamins  
RL: BIOL (Biological study)  
(oxygen **radical damage** to phycoerythrin protection by, in human plasma, structure in relation to)

IT **Albumins**, biological studies  
Deoxyribonucleic acids  
Ovalbumins  
Proteins, biological studies  
RL: BIOL (Biological study)  
(oxygen **radical damage** to phycoerythrin response to, in humans)

IT Named reagents and solutions  
RL: BIOL (Biological study)  
(Dulbecco's modified Eagle's, oxygen **radical damage** to phycoerythrin protection by, in human plasma, structure in relation to)

- to)
- IT Neurohormones  
RL: BIOL (Biological study)  
(neurotransmitters, oxygen **radical damage** to  
phycoerythrin protection by, in human plasma, structure in relation to)
- IT Molecular structure-biological activity relationship  
(oxygen radical formation-inhibiting, of protective agents, screening  
**assay** for)
- IT Phycoerythrins  
RL: BIOL (Biological study)  
(B-, oxygen **radical damage** to, in human plasma,  
protective agent screening in relation to)
- IT 50-67-9, Serotonin, biological studies 50-81-7, L-Ascorbic acid,  
biological studies 50-99-7, Glucose, biological studies 51-41-2,  
Norepinephrine 51-43-4, Epinephrine 51-45-6, Histamine, biological  
studies 51-61-6, Dopamine, biological studies 53-57-6, NADPH  
53-59-8, NADP+ 59-43-8, Thiamine, biological studies 59-67-6,  
Nicotinic acid, biological studies 59-92-7, biological studies  
63-68-3, Methionine, biological studies 69-93-2, biological studies  
71-44-3, Spermine 85-61-0, Coenzyme A, biological studies 85-87-0,  
Pyridoxamine 110-60-1, Putrescine 121-44-8, Triethylamine, biological  
studies 146-17-8, Riboflavin 5'-(dihydrogen phosphate) 306-08-1  
541-15-1, Carnitine 7365-45-9, HEPES 56305-04-5, Trolox  
RL: BIOL (Biological study)  
(oxygen **radical damage** to phycoerythrin protection  
by, in human plasma, structure in relation to)
- IT 9001-63-2, Lysozyme  
RL: BIOL (Biological study)  
(oxygen **radical damage** to phycoerythrin response  
to, in humans)
- IT 7782-44-7D, Oxygen, **radicals**  
RL: BIOL (Biological study)  
(phycoerythrin **damage** by, in human plasma, protective agent  
screening in relation to)

L25 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1989:107680 HCAPLUS

DOCUMENT NUMBER: 110:107680

TITLE: Oxidative damage to DNA and deoxyribose by  
.beta.-lactam antibiotics in the presence of iron and  
copper salts

AUTHOR(S): Quinlan, Gregory J.; Gutteridge, John M. C.

CORPORATE SOURCE: Div. Chem., Natl. Inst. Biol. Stand. Control, Potters  
Bar/Herts., EN6 3QG, UK

SOURCE: Free Radical Res. Commun. (1988), 5(3), 149-58

CODEN: FRRCEX; ISSN: 8755-0199

DOCUMENT TYPE: Journal

LANGUAGE: English

AB .beta.-Lactam antibiotics in the presence of certain metal ions damage  
deoxyribose and DNA with the release of thiobarbituric acid-reactive  
material. This damage can be substantially prevented by catalase, metal  
chelators and some scavengers of the hydroxyl radical. Ferric salts in  
the presence of certain .beta.-lactam antibiotics were effective in  
degrading deoxyribose but they did not appear to damage DNA. In contrast  
copper salts and .beta.-lactam antibiotics were extremely effective in  
damaging both DNA and deoxyribose.

CC 1-5 (Pharmacology)

IT **Albumins**, biological studies

RL: BIOL (Biological study)

(oxidative damage to deoxyribose and DNA by .beta.-lactam antibiotics

in presence of **metal** salts response to)  
 IT 7782-44-7D, Oxygen, **radicals**  
 RL: BIOL (Biological study)  
 (deoxyribose and DNA **damage** from .beta.-lactam antibiotics in  
 presence of **metal** salts)  
 IT 57-13-6, Urea, biological studies 62-56-6, Thiourea, biological studies  
 64-18-6, Formic acid, biological studies 65-85-0, Benzoic acid,  
 biological studies 69-65-8, Mannitol 70-51-9, Desferrioxamine  
 9001-05-2, Catalase 9054-89-1, Superoxide dismutase  
 RL: BIOL (Biological study)  
 (oxidative damage to deoxyribose and DNA by .beta.-lactam antibiotics  
 in presence of **metal** salts response to)

L25 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1988:508420 HCAPLUS  
 DOCUMENT NUMBER: 109:108420  
 TITLE: Gastric mucosal lesions induced by hemorrhagic shock  
 in baboons. Role of oxygen-derived free radicals  
 AUTHOR(S): Von Ritter, C.; Hinder, R. A.; Oosthuizen, M. M. J.;  
 Svensson, L. G.; Hunter, S. J. S.; Lambrecht, H.  
 CORPORATE SOURCE: Dep. Surg., Univ. Witwatersrand, Johannesburg, S. Afr.  
 SOURCE: Dig. Dis. Sci. (1988), 33(7), 857-64  
 CODEN: DDSCDJ; ISSN: 0163-2116  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The role of oxygen-derived free radicals during ischemia and reperfusion  
 in the prodn. of acute damage to the gastric mucosa of baboons was examd.  
 The protective effect of the xanthine oxidase inhibitor, allopurinol, the  
 superoxide scavenger, superoxide dismutase (SOD), and a long-acting  
 SOD-albumin was detd. A similar pattern of tissue damage was found at the  
 end of ischemia in all three (allopurinol + SOD, SOD-albumin, and control)  
 groups. Thirty minutes after reperfusion, severe mucosal damage (grade 3)  
 increased only in the untreated control. In the two treated groups, grade  
 3 damage remained unchanged during reperfusion and a decrease in the  
 percentage of moderate damage (grade 2) was seen. Both GSH and GSSG  
 tissue concns. were lower in the untreated controls as compared to the  
 scavenger-treated groups, making it questionable whether GSH/GSSG tissue  
 levels adequately reflect oxidative stress. Thus, the generation of  
 oxygen-derived free radicals produces mucosal damage and prevents the  
 restitution of moderate mucosal damage during reperfusion. In ischemia,  
 factors other than free radicals seem to be responsible for mucosal  
 damage. The protective effect of allopurinol and SOD was not mediated by  
 changes in gastric mucosal blood flow.

CC 14-7 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 1

IT Ischemia  
 (oxygen-derived **free radicals** mediation of  
**damage** during and after, in stomach, superoxide dismutase-  
**albumin** conjugate therapy in relation to)

L25 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1987:472274 HCAPLUS  
 DOCUMENT NUMBER: 107:72274  
 TITLE: Effect of **free radical** scavengers  
 and **metal** ion chelators on hydrogen peroxide  
 and phenylhydrazine induced red blood cell lipid  
 peroxidation  
 AUTHOR(S): Einsele, Hermann; Clemens, Michael R.; Wegner, Ulrike;  
 Waller, Hans Dierck  
 CORPORATE SOURCE: Med. Klin., Eberhard Karls Univ. Tuebingen, Tuebingen,



SOURCE: D-7400, Fed. Rep. Ger.  
Free Radical Res. Commun. (1987), 3(1-5), 257-63  
CODEN: FRRCEX; ISSN: 8755-0199

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Desferrioxamine a well-known Fe chelator decreased H<sub>2</sub>O<sub>2</sub>- and phenylhydrazine-induced lipid peroxidn. of red blood cell membranes assessed by hydrocarbon gas release and loss of polyunsatd. fatty acids. The OH scavengers like mannitol and thiourea and proteins like albumin were unable to reduce peroxidative reactions. Addn. of uric acid (in an unphysiol. concn. of 5 mM) to the incubation medium resulted in a slight redn. in H<sub>2</sub>O<sub>2</sub>/phenylhydrazine mediated break-down of arachidonic (20:4) and docosahexenoic acid (22:6) in the erythrocyte membrane and consequently in a decreased alkane release and hemolysis.

CC 4-3 (Toxicology)

IT **Albumins**, biological studies  
RL: BIOL (Biological study)  
(**free radical** induction of lipid peroxidn. response to, **radicals** scavengers in relation to)

IT Erythrocyte  
(lipid peroxidn. in, by **free radicals**, **radical** scavengers effect on)

IT Peroxidation  
(of lipids, hydrogen peroxide and phenylhydrazine induction by, in erythrocyte, **free radicals** scavengers effect on)

IT Lipids, biological studies  
RL: BIOL (Biological study)  
(peroxidn. of, hydrogen peroxide and phenylhydrazine induction of, in erythrocyte, **free radical** scavenger effect on)

IT 62-56-6, Thiourea, biological studies 64-17-5, Ethanol, biological studies 69-65-8, Mannitol 69-93-2, Uric acid, biological studies  
RL: BIOL (Biological study)  
(**free radical** induction of lipid peroxidn. response to, **radicals** scavengers in relation to)

IT 100-63-0, Phenylhydrazine  
RL: BIOL (Biological study)  
(lipid peroxidn. by, in erythrocyte, **free radicals** scavengers effect on)

IT 7722-84-1, Hydrogen peroxide, biological studies  
RL: BIOL (Biological study)  
(lipid peroxidn. induction by, in erythrocyte, **free radicals** scavengers effect on)

L25 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1986:223142 HCAPLUS

DOCUMENT NUMBER: 104:223142

TITLE: Role of some **free radicals** (sulfhydryl groups) in immune reactions and barrier function of spermatozoa membrane

AUTHOR(S): Kolinkoeva, A.

CORPORATE SOURCE: Inst. Biol. Immunol. Reprod. Dev. Org., Sofia, 1113, Bulg.

SOURCE: Dokl. Bolg. Akad. Nauk (1986), 39(2), 129-32  
CODEN: DBANAD; ISSN: 0366-8681

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The role and significance of SH groups, autoxidants, and other physiol.-active substances in antigen-antibody reactions was studied. Reactions among spermatozoa and antispermatozoal serum were used as a model system. Cysteine, serine, and dehydrocortisone enhanced the immune

reactions, but albumin, cholesterol, .alpha.-tocopherol, and .beta.-carotene suppressed the immune reactions.

CC 15-3 (Immunochemistry)  
 ST **antibody** antigen interaction sulfhydryl  
 IT **Albumins**, blood serum  
 RL: BIOL (Biological study)  
 (antibody-antigen reactions inhibition by)  
 IT **Antibodies**  
 RL: BIOL (Biological study)  
 (antigen reactivity with, sulfhydryl groups role in and autoxidants effect on)  
 IT Immunosuppressants  
 (autoxidants as, of **antibody**-antigen interactions)  
 IT Mercapto group  
 (in **antibody**-antigen reactions)  
 IT 52-90-4, biological studies 56-45-1, biological studies  
 RL: BIOL (Biological study)  
 (antibody-antigen interaction response to)  
 IT 16574-04-2  
 RL: BIOL (Biological study)  
 (antibody-antigen interaction stimulation by)  
 IT 57-88-5, biological studies 59-02-9 7235-40-7  
 RL: BIOL (Biological study)  
 (antibody-antigen interactions inhibition by)

L25 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1985:199930 HCAPLUS

DOCUMENT NUMBER: 102:199930

TITLE: Age pigments and **free radicals**:  
 fluorescent lipid complexes formed by iron- and copper-containing proteins

AUTHOR(S): Gutteridge, John M. C.

CORPORATE SOURCE: Div. Antibiot. Chem., Natl. Inst. Biol. Stand.  
 Control, Hempstead/London, NW3 6RB, UK

SOURCE: Biochim. Biophys. Acta (1985), 834(2), 144-8  
 CODEN: BBACAQ; ISSN: 0006-3002

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Heme and non-heme Fe-contg. proteins stimulate lipid peroxidn. with the formation of fluorescent lipid complexes. This process requires the presence of lipid hydroperoxides which release ferrozine-reactive Fe from heme-contg. proteins. Stimulation of lipid peroxidn. by the released Fe is inhibited by the Fe chelator desferrioxamine. Cu<sup>2+</sup>, although more stimulatory towards fluorescent lipid complex formation than Fe<sup>2+</sup>, does not stimulate lipid peroxidn. when tightly bound at the active center of proteins, but is reactive when loosely bound to albumin and histidine.

CC 6-5 (General Biochemistry)  
 Section cross-reference(s): 13

ST age pigment lipid peroxidn **metalloprotein**; copper protein lipid peroxidn age pigment; iron protein lipid peroxidn age pigment; radical lipid age pigment **metalloprotein**

IT **Albumins**, blood

RL: BIOL (Biological study)  
 (copper complexes, lipid peroxidn. stimulation by, age pigment formation in)

L25 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1976:587540 HCAPLUS

DOCUMENT NUMBER: 85:187540

TITLE: Spin labeled compounds for use in forensic analysis

INVENTOR(S): Goldstein, Avram; Leute, Richard K.; Ullman, Edwin F.  
 PATENT ASSIGNEE(S): Syva Co., USA  
 SOURCE: U.S., 46 pp. Continuation of U.S. 3,853,914.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3966744	A	19760629	US 1974-482542	19740624
US 3690834	A	19720912	US 1971-141516	19710510
FR 2121723	A5	19720825	FR 1972-687	19720110
FR 2121723	B1	19730629		
US 3853914	A	19741210	US 1972-270108	19720710
PRIORITY APPLN. INFO.:			US 1971-105535	19710111
			US 1971-141516	19710510
			US 1972-270108	19720710

AB Spin labeled compds. (ligand analogs) for use in forensic immunoassay were prepd. by modifying biol. active compds. or structural analogs and coupling them with a stable free radical compd. The ligand analog is recognizable by receptor mol., usually on antibody, and can compete with a biol. active mol. (ligand) for the receptor site in a way which allows the biol. active mol. to be assayed spectrometrically. For example, 2 mmoles amphetamine (I) [300-62-9] in 20 ml MeOH was treated with 106 mg Na<sub>2</sub>CO<sub>3</sub> [497-19-8] and 321 mg 3-(2'-iodoacetamido)-2,2,5,5-tetramethyl-1-pyrrolidiny-1-oxyl [27048-01-7] to give 187 mg 3-(N-(1'-phenyl-2'-propyl)glycinamido)-2,2,5,5-tetramethylpyrrolidiny-1-oxyl (II) [41370-71-2]. The Et<sub>2</sub>O ext. of a soln. of 3.68 g amphetamine sulfate [60-13-9] in 80 ml 0.5N NaOH was evapd., and the residue was dissolved in 50 ml benzene and treated with 3 ml diisopropylethylamine [7087-68-5] and 2.2 ml Et bromoacetate [105-36-2] to give the amino ester. The ester was dissolved in 50 ml 1:1 MeOH-1N NaOH, and the soln. was concd., and treated with HCl to pH 6 to give 900 mg N-carboxymethyl amphetamine [7738-39-8]. A suspension of the acid (700 mg) in 50 ml dry dioxane was treated with 20 ml of 12.5% phosgene in benzene, and the mixt. was evapd., redissolved in 20 ml/dry dioxane, and added over .5 hr to 2 g bovine serum albumin in 100 ml 2% NaHCO<sub>3</sub> at 0.degree.. After 24 hr at 0.degree. and 18 hr at room temp., the reaction mixt. was dialyzed for 2 days against 35 l H<sub>2</sub>O at 0.degree., and lyophilized, giving 1.91 g conjugate contg. .apprx.76 I units per unit of albumin. For urine anal. for I, 25 .mu.l urine was mixed with 2.5 .mu.l 0.2M Na<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub> and added to a mixt. of 22 .mu.l I antibody (.gamma.-globulin), 144 .mu.l 2M pH8 borate buffer, and 99 .mu.l saline. Five .mu.l of a soln. of 105 .mu.l H<sub>2</sub>O and 160 .mu.l 2.8 .times. 10<sup>-5</sup>M I soln. was added, and the soln. was examd. by ESR spectroscopy. The method detected I concns. in the range of 0.7-1.5 .mu.g/ml. It also detected several other drugs with structures similar to I.

IC C07D451-12

NCL 260292000

CC 4-2 (Toxicology)

Section cross-reference(s): 1

IT **Albumins**, blood serum

RL: BIOL (Biological study)

(bovine, ligand analogs conjugation with)

IT 1-Piperidineacetic acid, 3-ethyl-2,6-dioxo-3-phenyl-, **albumin** conjugates

1-Piperidineacetic acid, 4-(ethoxycarbonyl)-4-phenyl-, **albumin** conjugates

1-Pyrrolidinyloxy, 3-[[9-(dimethylamino)-1,6-dioxo-7,7-

- diphenyldecyl]amino]-2,2,5,5-tetramethyl-, **albumin** conjugates  
 2-Butenoic acid, 4-[hexahydro-5-(1-methylbutyl)-2,4,6-trioxo-5-pyrimidinyl]-, **albumin** conjugates  
 4-Piperidinecarboxylic acid, 1-methyl-4-phenyl-, bovine serum **albumin** conjugates  
 8-Azabicyclo[3.2.1]octane-2-carboxylic acid, 3-hydroxy-8-methyl-, **albumin** conjugates, [1R-(exo,exo)]-  
 8-Azabicyclo[3.2.1]octane-8-acetic acid, 3-(benzoyloxy)-2-(methoxycarbonyl)-, **albumin** conjugates, [1R-(exo,exo)]-  
 Acetic acid, [4-(2-aminopropyl)phenoxy]-, **albumin** conjugates  
 Acetic acid, [4-[2-(methylamino)propyl]phenoxy]-, **albumin** conjugates  
 Acetic acid, [4-[2-[(trifluoroacetyl)amino]propyl]phenoxy]-, anhydride with carbonochloridic acid, **albumin** conjugates  
 Acetic acid, [[(17.beta.)-17-hydroxyestra-1,3,5(10)-trien-3-yl]oxy]-, **albumin** conjugates  
 Acetic acid, [[[17.beta.)-3,17-dihydroxyestra-1,3,5(10)-trien-6-ylidene]amino]oxy]-, **albumin** conjugates  
 Benzenebutanoic acid, .beta.-(methylamino)-, **albumin** conjugates  
 Benzenediazonium, 4-[(2-carboxy-3-hydroxy-8-azabicyclo[3.2.1]oct-8-yl)methyl]-, **albumin** conjugates, [1R-(exo,exo)]-  
 Benzenediazonium, 4-[(2-carboxy-8-methyl-8-azabicyclo[3.2.1]oct-3-yl)oxy]carbonyl]-, hydroxide, inner salt, **albumin** conjugates, [1R-(exo,exo)]-  
 Benzenediazonium, 4-[[3-hydroxy-2-(methoxycarbonyl)-8-azabicyclo[3.2.1]oct-8-yl]methyl]-, **albumin** conjugates, [1R-(exo,exo)]-  
 Estrane, acetic acid deriv., **albumin** conjugates  
 Estrane, acetic acid deriv., **albumin** conjugates  
 L-Lysine, homopolymer, hydrobromide, carboxymethylmorphine conjugates  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 IT Glycine, N-(1-methyl-2-phenylethyl)-, **albumin** conjugates  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of and **antibody** formation by)  
 IT 7738-39-8P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and **albumin** conjugation of)  
 IT 60-13-9  
 RL: RCT (Reactant)  
 (reaction of, with esters and **free radical** spin-labeling compds.)  
 IT 70-34-8 77-17-8 300-62-9  
 RL: RCT (Reactant)  
 (reaction of, with **free radical** spin-labeling compds.)  
 IT 57-27-2, reactions  
 RL: RCT (Reactant)  
 (with **free radical** spin-labeling compds.)

L25 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1968:10041 HCAPLUS

DOCUMENT NUMBER: 68:10041

TITLE: Reaction of serum albumin and glycyltryptophan free radicals with radioprotective substances

AUTHOR(S): Sapezhinskii, I. I.; Dontsova, E. G.

CORPORATE SOURCE: Inst. Khim. Fiz., Moscow, USSR

SOURCE: Biofizika (1967), 12(5), 794-8

CODEN: BIOFAI

DOCUMENT TYPE: Journal

LANGUAGE: Russian

AB Effective consts. (1/mol. sec.) of interaction rates with free radicals of protein (Kb) and with glycytryptophan are resp. listed for radioprotective substances: .beta.-mercaptoethylamine 4.6, 10.6; thiourea 2.9, 4.4; cysteine-HCl 2.6, 10.4; aminoethylisothiuronium-HBr 1.7, 3.3; aminopropylisothiuronium-HBr 1.6, 1.8; reduced glutathione 1.3, 3.5; propyl gallate 1.2, 0.4; Na diethyldithiocarbamate (I) 3.4 .times. 10<sup>3</sup>, 10<sup>3</sup>. The Kb with cysteine did not depend on protein concn. There is no correlation between the above-listed consts. and the reactivity of the compds. with protein. Mechanism of I reaction with protein-free radicals differed from the mechanism of the other compds. The protein under study was bull serum albumin.

CC 5 (Radiation Biochemistry)

IT **Albumins**, blood serum

RL: BIOL (Biological study)  
 (radicals (free) of, reaction with radiation-  
 damage protective agents)

=> dhis

DHIS IS NOT A RECOGNIZED COMMAND

=> d his

(FILE 'WPIDS' ENTERED AT 09:31:09 ON 03 DEC 2001)  
DEL HIS Y

FILE 'REGISTRY' ENTERED AT 09:33:11 ON 03 DEC 2001

L1 88 S ^DAHK/SQSP  
L2 19 S L1 AND SQL=4

FILE 'HCAPLUS' ENTERED AT 09:34:32 ON 03 DEC 2001

L3 13 S L2  
L4 4 S L3 AND RADICAL?  
L5 4 S L1 AND RADICAL?  
L6 4 S L4 OR L5

=> fil wpids

FILE 'WPIDS' ENTERED AT 10:22:55 ON 03 DEC 2001  
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FILE LAST UPDATED: 29 NOV 2001 <20011129/UP>  
MOST RECENT DERWENT UPDATE 200170 <200170/DW>  
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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<http://www.derwent.com/chemistryresource/index.html> <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,  
SEE <http://www.derwent.com/dwpi/updates/dwpicov/index.html> <<<

=> d his

(FILE 'WPIDS' ENTERED AT 10:12:12 ON 03 DEC 2001)

DEL HIS Y

L1 6073 S ALBUMIN?  
L2 13382 S FREE (3A) RADICAL#  
L3 44 S L1 AND L2  
L4 4 S L3 AND METAL?  
L5 25638 S MARKER#  
L6 2 S L3 AND L5  
L7 97 S L1 (4A) (MODIF? OR ALTER? OR DAMAG?)  
L8 2 S L2 AND L7  
L9 531 S OXIDATIVE (4A) (DAMAG? OR STRESS?)  
L10 14 S L9 AND L1  
L11 1 S L10 AND L7  
L12 1028 S ATOMIC (3A) SPECT?  
L13 1 S L3 AND L12  
L14 1 S L12 AND L9  
L15 0 S DAHK  
L16 9 S ASP ALA HIS LYS  
L17 1 S ASPARTIC ACID (2W) ALANINE (2W) HISTIDINE (2W) LYSINE  
L18 10 S L16 OR L17  
L19 3 S L18 AND L1  
L20 6 S L6 OR L11 OR L13 OR L14 OR L19  
L21 783099 S V OR AS OR CO OR SB OR CR OR MO OR MN OR BA OR ZN OR NI OR H  
L22 11 S L3 AND L21  
L23 654085 S VANADIUM OR ARSENIC OR COBALT OR ANTIMONY OR CHROMIUM OR MOLY  
L24 5 S L23 AND L3  
L25 14 S L22 OR L24  
L26 5 S L20 NOT L25  
L27 13 S L25 NOT L20

FILE 'WPIDS' ENTERED AT 10:22:55 ON 03 DEC 2001

=> d .wp 120 1-6;d .wp 127 1-13

L20 ANSWER 1 OF 6 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
AN 2000-579163 [54] WPIDS  
DNN N2000-428604 DNC C2000-172361  
TI New isolated peptide which mimics a carbohydrate epitope is useful for

neuroprotection.

DC A96 B04 D16 S03

IN HERZBERG, U; NEUBERGER, T J; SCHACHNER, M; SIMON, M

PA (ACOR-N) ACORDA THERAPEUTICS

CYC 90

PI WO 2000050447 A1 20000831 (200054)\* EN 212p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES

FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS

LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL

TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000028841 A 20000914 (200063)

ADT WO 2000050447 A1 WO 2000-US4730 20000224; AU 2000028841 A AU 2000-28841 20000224

FDT AU 2000028841 A Based on WO 200050447

PRAI US 2000-511956 20000223; US 1999-121327P 19990224; US 1999-256970

19990224; US 1999-155492P 19990923; US 1999-404431 19990923

AB WO 200050447 A UPAB: 20011129

NOVELTY - An isolated peptide (I) which mimics the carbohydrate epitope GlcA beta 1-->3Gal beta 1-->4GlcNAc or sulphate-3GlcA beta 1-->3Gal beta 1-->4GlcNAc is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated peptide comprising sequence (1) - (8) or one of the twelve 15 - 17 amino acid sequences provided in the specification;

(2) a method (M1) for promoting neural growth and/or remyelination and/or neuroprotection in vivo in the central nervous system (CNS) comprising administering (I), which is capable of overcoming inhibitory molecular cues found on glial cells and myelin and promoting neural growth;

(3) a method (M2) for enhancing memory comprising administering (I) to the brain of a mammal;

(4) a method (M3) for increasing synaptic efficacy in the CNS of a mammal comprising administering (I);

(5) a method (M4) for promoting neuroprotection and/or neuronal survival comprising administering (I);

(6) a method (M5) for inhibiting axonal cell death and enhancing myelination and remyelination in the CNS comprising administering (I), which is capable of overcoming inhibitory molecular cues found on glial cells and myelin and promoting neural growth;

(7) a DNA sequence (II) which encodes (I);

(8) a unicellular host transformed with (II);

(9) a cloning and expression vector comprising (II);

(10) a method (M6) for detecting the presence or activity of (I)

comprising:

(a) contacting a sample with a binding partner; and

(b) detecting whether binding has occurred, where detection of binding indicates the presence or activity of the peptide;

(11) a test kit for the demonstration of a molecule capable of binding GlcA beta 1-->3Gal beta 1-->4GlcNAc or sulphate-3GlcA beta 1-->Gal beta 1--> 4GlcNAc in a eukaryotic cellular sample comprising:

(a) a predetermined amount of a detectably (I);

(b) other reagents; and

(c) directions for use;

(12) a method (M7) for testing the ability of a drug or other entity to mimic (I) comprises:

(a) adding CNS neurons to a cell culture system;

(b) adding the drug or other entity to a cell culture system;

(c) measuring the neuronal outgrowth of the CNS neurons; and



(d) correlating a difference in the level of neuronal outgrowth of cells in the presence of the drug relative to a control culture to which no drug is added;

(13) a pharmaceutical composition comprising (I);

(14) a method (M8) for preventing, ameliorating or blocking viral infection comprising administering (I); and

(15) a method (M9) for preventing, ameliorating or blocking neuropathy comprising administering (I), where the neuropathy is viral mediated, immune mediated or the result of trauma.

X1a-X2a-X3a-X4a-X5a-Leu/Val-X6a-X7a-X8a-X9a-X10a-X11a-X12a-X13a-X14a (1);

Phe-Leu-His-Thr-Arg-Leu-X1b-X2b-X3b-X4b-X5b-X6b-X7b-X8b-X9b (2);

Phe-Leu-His-Thr-Arg-Leu-Phe-Val-X1c-X2c-X3c-X4c-X5c-X6c-X7c (3);

Phe-Leu-His-Thr-Arg-Leu-Phe-Val-Ser-Asp-Trp-Tyr-His-Thr (4);

Phe-Leu-His-Thr-Arg-Leu-Phe-Val (5);

Thr-Arg-Leu-Phe-Arg-(Val/Phe) (6);

Thr-Arg-Leu-Phe-(Arg)-Val (7); and

Thr-Arg-Leu-Phe (8).

Where:

X1a = Thr, Ser, Ala or Pro;

X2a = Leu, Ile, Val, Met, Phe, His, Trp or Asn;

X3a = Thr, Ser, Ala, His, Tyr, Phe, Trp, Asn, Asp or Glu;

X4a = Arg, Gln, Lys, Thr, Ser or Ala;

X5a = Val, Ile, Leu, Met, Arg, Gln or Lys;

X6a = Thr, Ser, Ala, Tyr, Phe, His, Trp, Asn, Leu, Ile, Val or Met;

X7a = Asp, Glu, Val, Leu, Ile, Met, Phe, Tyr, His, Trp or Asn;

X8a = Val, Ile, Leu, Met, Ser, Ala, Thr, Arg, Gln or Lys;

X9a = Tyr, Phe, His, Trp, Asp, Glu, Ile, Val, Leu, Met or Asn;

X10a = Arg, Gln, Lys, Trp, Tyr, Phe, His, Asn, Val, Ile, Leu, Met or

Gly;

X11a = Gly, Tyr, Phe, His, Trp, Asn, Ser, Ala, Thr, Ile, Val, Leu or

Met;

X12a = Arg, Gln, Lys, His, Asn, Tyr, Phe, Trp, Ile, Val, Leu or Met;

X13a = Leu, Val, Ile, Met, Thr, Ser or Ala;

X14a = Ser, Thr, Ala, Pro, Gly, Arg, Gln or Lys;

X1b = Thr, Ser, Ala, Tyr, Phe, His, Trp, Asn, Leu, Ile, Val or Met;

X2b = Asp, Glu, Val, Leu, Ile, Met, Phe, Tyr, His, Trp or Asn;

X3b = Val, Ile, Leu, Met, Ser, Ala, Thr, Arg, Gln or Lys;

X4b = Tyr, Phe, His, Trp, Asp, Glu, Ile, Val, Leu, Met or Asn;

X5b = Arg, Gln, Lys, Trp, Tyr, Phe, His, Asn, Val, Ile, Leu, Met or

Gly;

X6b = Gly, Tyr, Phe, His, Trp, Asn, Ser, Ala, Thr, Ile, Val, Leu or

Met;

X7b = Arg, Gln, Lys, His, Asn, Tyr, Phe, Trp, Ile, Val, Leu or Met;

X8b = Leu, Val, Ile, Met, Thr, Ser or Ala;

X9b = Ser, Thr, Ala, Pro, Gly, Arg, Gln or Lys;

X1c = Val, Ile, Leu, Met, Ser, Ala, Thr, Arg, Gln or Lys;

X2c = Tyr, Phe, His, Trp, Asp, Glu, Ile, Val, Leu, Met or Asn;

X3c = Arg, Gln, Lys, Trp, Tyr, Phe, His, Asn, Val, Ile, Leu, Met or

Gly;

X4c = Gly, Tyr, Phe, His, Trp, Asn, Ser, Ala, Thr, Ile, Val or Met;

X5c = Arg, Gln, Lys, His, Asn, Tyr, Phe, Trp, Ile, Val, Leu or Met;

X6c = Leu, Val, Ile, Met, Thr, Ser or Ala; and

X7c = Ser, Thr, Ala, Pro, Gly, Arg, Gln or Lys.

ACTIVITY - Nootropic; neuroprotective; antiparkinsonian.

No supporting biological data is given.

MECHANISM OF ACTION - None given.

USE - For enhancing memory for inhibiting the onset or progression, or treating the presence or consequences of Alzheimers disease or dementia. For inhibiting the development or onset or treating the

presence of apoptosis, necrosis, Parkinsons disease, multiple sclerosis and acute and chronic spinal cord injury (all claimed).  
Dwg.0/20

L20 ANSWER 2 OF 6 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
AN 2000-303843 [26] WPIDS  
DNN N2000-226961 DNC C2000-092353  
TI New method for the continuous detection of ischemic states comprises detecting and quantifying the existence of an alteration of the serum protein **albumin**.  
DC B04 D16 S03  
IN BAR-OR, D; LAU, E; WINKLER, J V  
PA (ISCH-N) ISCHEMIA TECHNOLOGIES INC  
CYC 90  
PI WO 2000020840 A1 20000413 (200026)\* EN 102p  
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
OA PT SD SE SL SZ TZ UG ZW  
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES  
FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS  
LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ  
TM TR TT TZ UA UG US UZ VN YU ZA ZW  
AU 9964095 A 20000426 (200036)  
EP 1125107 A1 20010822 (200149) EN  
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE  
ADT WO 2000020840 A1 WO 1999-US22905 19991001; AU 9964095 A AU 1999-64095  
19991001; EP 1125107 A1 EP 1999-951710 19991001, WO 1999-US22905 19991001  
FDT AU 9964095 A Based on WO 200020840; EP 1125107 A1 Based on WO 200020840  
PRAI US 1999-115392P 19990111; US 1998-102738P 19981002; US 1998-165581  
19981002; US 1998-165926 19981002  
AB WO 200020840 A UPAB: 20000531  
NOVELTY - A method (M1) for the continuous detection of ischemic states by detecting and quantifying the existence of an alteration of the serum protein **albumin**, is new.  
DETAILED DESCRIPTION - A method (M1) for the continuous detection of ischemic states by detecting and quantifying the existence of an alteration of the serum protein **albumin**, is new.  
M1 comprises:  
(a) contacting a biological sample containing **albumin** from the patient with an excess quantity of a metal ion salt, where the metal ion binds to the N-terminus of naturally occurring human **albumin**, to form a mixture containing bound metal ions and unbound metal ions  
(b) determining the amount of metal ions bound to the **albumin** N-terminus, and  
(c) correlating the amount of bound metal ions to a known value to determine the occurrence or non-occurrence of an ischemic event.  
INDEPENDENT CLAIMS are also included for the following:  
(1) A method (M2) for detecting the occurrence or non-occurrence of an ischemic event in a patient comprising:  
(a) detecting the amount of endogenous copper ions present in a purified **albumin** sample from the patient; and  
(b) correlating the quantity of copper ions present with a known value to determine the occurrence or non-occurrence of an ischemic event;  
(2) A method for ruling-out the existence of ischemia in a patient, where the patient possesses one or more cardiac risk factors, comprising:  
(a) application of M1 or M2 to the patient;  
(b) subjecting the patient to an exercise treadmill test followed by a second application of M1 or M2;  
(c) comparing the results of the two applications of the method;  
(3) A method for evaluation of a patient presenting with angina or angina-like symptoms to detect the occurrence or non-occurrence of a

myocardial infarction, comprising:

- (a) application of M1 or M2 to the patient;
- (b) application of an electrocardiographic test;
- (c) correlating the results of step (a) with the results of the electrocardiographic test to determine the occurrence or non-occurrence of a myocardial infarction.

(4) A method for supplementing electrocardiographic results to determine the occurrence or non-occurrence of an ischemic event, is similar to the method of (3), except step (c) comprises correlating the results of step (a) with the results of the electrocardiographic test to determine the occurrence or non-occurrence of an ischemic event;

(5) A method for comparing levels of ischemia in patients at rest and during exercise, comprising application of the following steps at designated times:

- (a) application of M1 or M2 at a first designated time;
- (b) administration of an exercise treadmill test followed by a second application of the same method employed in step (a);
- (c) comparing the results of step (a) with the results obtained in step (b); and
- (d) repeating steps (a) and (b) at additional designated times, where results obtained designated at each designated time are compared;

(6) An immunoassay diagnostic kit for an ischemic event comprising:

- (a) an excess quantity of a metal ion to mix with a patient sample which comprises naturally-occurring **albumin** and optionally **albumin** N-terminal derivatives, the naturally-occurring **albumin** forming a complex with the metal ion;

- (b) a first elongated solid support having a first and a second end, the first end having a filter for application of the patient sample mixture, an area of immobilized antibody to the **albumin**-metal complex between the first end the second end, and an area of immobilized ligand to **albumin** proximate the second end, where after application of the mixture of patient sample and metal ion to the filter, the **albumin**-metal complex is immobilized at the area of immobilized antibody, and the **albumin** N-terminal derivatives migrate and bind to the **albumin** ligand proximate the second end;

(7) A metal affinity diagnostic kit for an ischemic event comprising a first elongated solid support having a first and a second end, the first end having a filter for application of a patient sample, an area of immobilized metal ion between the first and the second end, and an area of immobilized ligand to naturally occurring **albumin** or **albumin** N-terminal derivatives proximate the second end;

(8) A ligand directed to an epitope at the N-terminus of the **albumin** N-terminal derivative which lacks four, three, two or one N-terminal amino acids of a 585 amino acid sequence (I) defined in the specification;

(9) A ligand to an epitope at the N-terminus of a 585 amino acid sequence (II) defined in the specification;

(10) A calibrator composition comprising a predetermined molar ratio of naturally occurring albumin and a metal that complexes to the N-terminus of the albumin, where the complexed albumin and unbound albumin form when the composition is in aqueous solution, where the ratio is between 0.1:1 and 1:0.1;

(11) A method of calibrating an analyzer that detects or measures an ischemic event according to M1, comprising applying the solution of (10) to the analyzer to determine the amount of metal ions (preferably copper) bound to the albumin N-terminus, where the predetermined ration of albumin to metal serves as a standard for calibration;

(12) A method of detecting an albumin N-terminal derivative which lacks four, three, two, or one N-terminal amino acids of (I), comprising contacting a sample comprising the derivative with the ligand of (8);

(13) A method of detecting an albumin N-terminal derivative which is acetylated at its N-terminal Asp residue of (II), comprising contacting a sample comprising the derivative with the ligand of (9); and

(14) A calibrator composition comprising a predetermined molar ratio of naturally occurring albumin and albumin N-terminal derivatives, where the ratio is between 0.1:1 and 1:0.1.

USE - The methods are useful for detection of ischemic states. The methods are also useful for distinguishing perioperative ischemia from ischemia caused by, amongst other things, myocardial infarctions and progressive coronary artery disease.

ADVANTAGE - The method is rapid.

Dwg.0/19

L20 ANSWER 3 OF 6 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 2000-303746 [26] WPIDS

DNN N2000-226916 DNC C2000-092265

TI Sensitive **marker** for detection of **free radical** damage comprising modified **albumin**, useful for detecting diseases associated with **free radicals** such as neurodegenerative diseases and cancers.

DC B04 S03

IN BAR-OR, D; LAU, E

PA (DIAG-N) DIAGNOSTIC MARKERS INC

CYC 88

PI WO 2000020454 A1 20000413 (200026)\* EN 36p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB  
GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU  
LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR  
TT UA UG US UZ VN YU ZA ZW

AU 9962793 A 20000426 (200036)

EP 1117686 A1 20010725 (200143) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
RO SE SI

ADT WO 2000020454 A1 WO 1999-US22746 19991001; AU 9962793 A AU 1999-62793  
19991001; EP 1117686 A1 EP 1999-950055 19991001, WO 1999-US22746 19991001

FDT AU 9962793 A Based on WO 200020454; EP 1117686 A1 Based on WO 200020454

PRAI US 1998-165961 19981002; US 1998-102962P 19981002

AB WO 200020454 A UPAB: 20000531

NOVELTY - A **marker** (I) for the detection of **free radical** damage, comprising **albumin** which is modified in a manner resulting in inhibition of metal binding capacity of the N-terminus, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method for detecting and quantifying (I) comprising:

(a) providing a biological sample containing **albumin**;

(b) providing a metal ion salt, where the metal ion is capable of binding to the N-terminus of unmodified **albumin**;

(c) contacting the biological sample with an excess quantity of the metal ion so that a mixture of bound and unbound ions is formed;

(d) determining the quantity of bound metal ions; and

(e) correlating the quantity of bound metal ions to a known value to determine the quantity of the **marker** present in the sample and to determine if the quantity is sufficient to indicate **free radical** damage;

(2) a method for detecting and quantifying (I) comprising:

(a) determining the quantity of copper ions present in a purified **albumin** sample; and

(b) correlating the quantity of the copper ions present in the sample with a known value to determine the quantity of the **marker** present in the sample and to determine if the quantity is sufficient to indicate **free radical** damage;

(3) a compound having the formula **Asp-Ala-His-Lys-R**, where R is any chemical group capable of providing a detectable signal when the compound is bound to a metal ion capable of binding to the N-terminus of unmodified human **albumin**;

(4) an antibody (Ab1) binding to (I)

(5) an antibody (Ab2) that binds to the peptide **Asp-Ala-His-Lys**;

(6) an immunological assay conducted using (I) as an antigen;

(7) an immunological assay using Ab1 or Ab2;

(8) a method of monitoring or assessing a disease or condition comprising detecting and quantifying (I); and

(9) a kit for detecting or quantifying (I).

USE - The methods are useful for detecting diseases associated with **free radicals** including Parkinson's, Alzheimer's, cataractogenesis, atherosclerosis, diabetes mellitus, ischemia-reperfusion injury and certain toxicities. (I) is useful as a biochemical tag, allowing for sensitive detection and measurement of the efficacy of clinical drugs and therapeutics which result in the generation of **free radicals** or which act to limit **free radical** damage.

ADVANTAGE - (I) is a **marker** for the existence and detection and/or measurement of **free radical** damage which is highly sensitive and present in a majority of human fluids and tissues.  
Dwg.0/0

L20 ANSWER 4 OF 6 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
AN 1993-076649 [09] WPIDS  
DNN N1993-058859 DNC C1993-033841  
TI Method for detection of ischaemic states - by contacting serum or plasma sample with metal ions (e.g. cobalt) capable of binding to thiol gps..  
DC B04 S03  
IN BAR-OR, D; SOLOMONS, C  
PA (DIAG-N) DIAGNOSTIC MARKERS INC; (ISCH-N) ISCHEMIA TECHNOLOGIES INC  
CYC 23  
PI WO 9303346 A1 19930218 (199309)\*  
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE  
W: AU BR CA JP KR NO  
AU 9223187 A 19930302 (199326)  
US 5227307 A 19930713 (199329) 6p  
PT 100724 A 19930930 (199342)  
US 5290519 A 19940301 (199409) 6p  
NO 9400256 A 19940125 (199415)  
EP 596925 A1 19940518 (199420) EN  
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE  
JP 06509645 W 19941027 (199502)  
BR 9206312 A 19950411 (199521)  
EP 596925 A4 19960214 (199639)  
AU 9710006 A 19970320 (199720)  
AU 705300 B 19990520 (199931)  
KR 239947 B1 20000115 (200116)  
JP 3194952 B2 20010806 (200147) 9p  
ADT WO 9303346 A1 WO 1992-US5668 19920710; AU 9223187 A AU 1992-23187  
19920710; US 5227307 A US 1991-736583 19910726; PT 100724 A PT 1992-100724  
19920724; US 5290519 A Div ex US 1991-736583 19910726, US 1993-16971  
19930212; NO 9400256 A WO 1992-US5668 19920710, NO 1994-256 19940125; EP

596925 A1 EP 1992-915563 19920710, WO 1992-US5668 19920710; JP 06509645 W  
WO 1992-US5668 19920710, JP 1993-503561 19920710; BR 9206312 A BR  
1992-6312 19920710, WO 1992-US5668 19920710; EP 596925 A4 EP 1992-915563  
; AU 9710006 A Div ex AU 1992-23187 19920710, AU 1997-10006 19970103; AU  
705300 B Div ex AU 1992-23187 19920710, AU 1997-10006 19970103; KR 239947  
B1 WO 1992-US5668 19920710, KR 1994-700225 19940125; JP 3194952 B2 WO  
1992-US5668 19920710, JP 1993-503561 19920710

FDT AU 9223187 A Based on WO 9303346; US 5290519 A Div ex US 5227307; EP  
596925 A1 Based on WO 9303346; JP 06509645 W Based on WO 9303346; BR  
9206312 A Based on WO 9303346; AU 705300 B Previous Publ. AU 9710006; JP  
3194952 B2 Previous Publ. JP 06509645, Based on WO 9303346

PRAI US 1991-736583 19910726; US 1993-16971 19930212

AB WO 9303346 A UPAB: 19990802

Detection of ischaemia in a patient comprises: (a) contacting a serum, plasma, fluid or tissue sample of the patient with metal ions, capable of binding to thiol gps. in the sample, to form a mixt. contg. sample bound metal ions and non-sample bound metal ions; and (b) detecting the amt. of non-sample bound metal ions to determine the amt. of thiol gps. in the sample.

Also claimed is a kit, for detecting the presence of an ischaemic event, comprising a metal salt and a colour-forming cpd. capable of forming a coloured cpd. with the metal salt.

USE/ADVANTAGE - In patients who have experienced an ischaemic event, the no. of thiol gps. in the proteins contained in the serum, plasma, fluid or tissue of the patient is reduced due to oxidn. by OH and peroxide radicals. The process quantifies protein-bound thiol gps. in a sample as a measure of **oxidative damage** to the sample due to the ischaemic event. The free metal ions remaining after complexation may be detected by conventional methods. The samples may be compared with samples from healthy patient

Dwg.0/0

L20 ANSWER 5 OF 6 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1987-291654 [41] WPIDS

DNC C1987-123876

TI Measuring **oxidative damage** to cells - by chemiluminescence using complex of luminescer and serum **albumin**.

DC B04 D16

IN KIEI, J L

PA (MCLA-N) MCLAS TECHNOL INC

CYC 13

PI WO 8705941 A 19871008 (198741)\* EN 65p

RW: AT BE CH DE FR GB IT LU NL SE

W: AU DK JP

AU 8773974 A 19871020 (198803)

ADT WO 8705941 A WO 1987-US686 19870324

PRAI US 1986-844001 19860325

AB WO 8705941 A UPAB: 19930922

**Oxidative damage** to living cells is measured by contacting the cells with a complex of a luminescer (I) and serum **albumin** (II), where (I) is non-covalently bonded to (II), and triggering a light-generating reaction.

(I) is luminol and (II) is bovine serum **albumin** (BSA). The complex may also contain a heme protein (III) in the form of a conjugate formed from (I), (II), (III) and a polyamino cpd. (esp. lysine). The conjugate may be crosslinked with a bifunctional cpd., e.g. glutaraldehyde. After contacting the cells with the complex, they are treated with a reducing agent (esp. KBH4) and luminescence is triggered by adding a base. When the complex contains (III), luminescence may also be triggered by heating.

USE/ADVANTAGE - The process may be used as a diagnostic tool for detecting exposure to exogenous oxidants, ionising radiation or hyperthermia or for detecting deficiencies in free-radical-scavenging enzymes. Use of (II) eliminates the need for an oxidase-peroxidase system. The (I)-(II) complex is bound by cell-surface aldehyde gps. (formed by peroxidative damage), and the bound complex produces so much more luminescence than the unbound complex that a homogeneous assay may be performed without a washing step.  
0/14

L20 ANSWER 6 OF 6 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1966-30621F [00] WPIDS  
 TI Organic molecules providing **free radicals** for tagging of biomolecules by electron-spin resonance - A. of formula - where C1 and C2 are tert. C atoms.  
 DC B04 E13 J04  
 PA (SYNT) SYNVAR ASSOC  
 CYC 6  
 PI FR 1501115 A (196800)\*  
 GB 1169872 A (196801)  
 US 3453288 A (196801)  
 US 3481952 A (196801)  
 US 3489522 A (197002)  
 CA 839265 A (197016)  
 JP 45010138 B (197016)  
 JP 46019520 B (197121)  
 DE 1620411 A 19700430 (198422)  
 PRAI US 1965-512793 19651209  
 AB FR 1501115 A UPAB: 19930831  
 Organic molecules providing **free radicals** for tagging of biomolecules by electron-spin resonance:-  
 A. of formula:-  
 where C1 and C2 are tert. C atoms bound directly to c or fluorine atoms; A is at least one organic group having a total of 6 valencies available for bonding to atoms C1 and C2 and contains a functional group (not 2,4-dinitrophenyl) capable of forming a linkage with a biol. active molecule.  
 B. Esp. of formula  
 where R', R2, R3, R4 = lower alkyl, B = alkylene which completes the heterocyclic ring; X = organic group contng. a functional group (not 2,4-dinitrophenyl) capable of forming a linkage with a biol. active molecule, esp. isocyanate, isothiocyanate or a maleimide nucleus.  
 Tagging of various parts of molecules with specific **markers** allows one to follow the course of biol. reactions and to elucidate chemical structure. The **markers** are stable in aqs. media. For example the action of pepsin on bovine serum **albumin** may be followed by tagging the **albumin** with 2,2,5,5-tetramethyl-3-isocyanatopyrrolidine-1-oxide. Fluorescent **markers** may be incorporated in the molecule of the electron-spin resonance **marker**.

L27 ANSWER 1 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 2001-483075 [52] WPIDS  
 DNC C2001-144788  
 TI Gel-based medium composition useful for storage and transport of cell

samples, comprises a cell maintenance and preservation medium and a gelling agent.

DC B04 D16 D22

IN BAUST, J G; BAUST, J M; VAN BUSKIRK, R

PA (BIOL-N) BIOLIFE SOLUTIONS INC

CYC 21

PI WO 2001050851 A2 20010719 (200152)\* EN 22p

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR

W: CA JP

ADT WO 2001050851 A2 WO 2001-US912 20010112

PRAI US 2001-176009 20010111; US 2000-176009P 20000114

AB WO 200150851 A UPAB: 20010914

NOVELTY - A gel-based medium composition contains at least one cell maintenance and preservation medium and at least one gelling agent, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for storing cell samples in a gel-based medium composition, comprising:

(a) warming the composition to melt the gelling agent;

(b) suspending cell samples in a cell preservation solution without a gelling agent;

(c) mixing the suspended cell samples with the warmed gel-based medium composition;

(d) cooling the cell samples to solidify the gelling agent; and

(e) transferring the cooled cell samples to a desired storage temperature, preferably -196 - 37 deg. C.

The cooled cell samples are transported in a gelled state.

USE - For storage and transport of cell samples in the form of organs, tissues, cell monolayer and single cells, which are obtained from plants, animals, fungi, microbes or humans at normothermic, hypothermic and cryopreservative temperature, preferably -196 - 37 deg. C (claimed).

ADVANTAGE - The composition protects the cell samples from the mechanical, physiological and biochemical stresses inherently associated with liquid preservation techniques. The gelled preservation media enables preservation of tissue in a semi-solid preservation matrix keeping the tissue structurally intact while affording the same protective benefits to the tissue as is conferred to individual cells and cell monolayers. The reduction in the external mechanical shipping forces experienced by the tissues shipped in the gel medium markedly improves tissue viability following preservation.

Dwg.0/8

L27 ANSWER 2 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 2001-407935 [43] WPIDS

DNC C2001-123484

TI Dialysis solution including a polyglycol osmotic agent, providing reduced dialysis time, and/or **free radical** scavenger reducing complications due to production of degradation products from gamma sterilization.

DC A96 B05

IN SIMON, J; STRICKLAND, A D; STROM, R M

PA (DOWC) DOW CHEM CO

CYC 90

PI WO 2001028544 A2 20010426 (200143)\* EN 10p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
NL OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CZ DE DK DM DZ

EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ LC LK LR

LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI

SK SL TJ TM TR TT TZ UA UG UZ YU ZA ZW

AU 2000078795 A 20010430 (200148)



ADT WO 2001028544 A2 WO 2000-US28523 20001013; AU 2000078795 A AU 2000-78795 20001013

FDT AU 2000078795 A Based on WO 200128544

PRAI US 1999-159810P 19991015

AB WO 200128544 A UPAB: 20011129

NOVELTY - A dialysis solution including a polyglycol osmotic agent having a molecular weight 500-20,000 daltons, provides an improved osmotic gradient resulting in reduced dialysis times and/or reduced volumes of required dialysis solution. Also **free radical** scavengers are used to reduce complications due to degradation products from gamma sterilization.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (a) use of the solutions for performing dialysis;
- (b) use of a filter to reduce introduction of bacteria into the peritoneal cavity; and
- (c) a dialysis solution comprising a **free radical** scavenger.

USE - For use in hemodialysis or peritoneal dialysis.

ADVANTAGE - Use of a **free radical** scavenger in the dialysis solution allows sterilization of the solution using gamma radiation with minimal damage to solution components while maintaining a physiological pH.

Dwg.0/0

L27 ANSWER 3 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 2000-572048 [53] WPIDS

DNC C2000-170525

TI Negatively charged microporous membrane, useful e.g. for recovering charged biomolecules from a gel, comprises porous substrate and crosslinked coating with pendant anionic groups.

DC A11 A14 A89 B04 D16 G02 J01 J04

IN HOU, C; KONSTANTIN, P; YANG, Y

PA (PALL) PALL CORP

CYC 90

PI WO 2000050160 A1 20000831 (200053)\* EN 33p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES

FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS

LT LU LV MA MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL

TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000033764 A 20000914 (200063)

ADT WO 2000050160 A1 WO 2000-US4745 20000225; AU 2000033764 A AU 2000-33764 20000225

FDT AU 2000033764 A Based on WO 200050160

PRAI US 1999-121668P 19990225

AB WO 200050160 A UPAB: 20001023

NOVELTY - Negatively charged microporous membrane (A) comprises a porous substrate (B) and a crosslinked coating (C) having pendant anionic groups.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) (A) having dynamic protein-binding capacity of at least 25 mg lysozyme/ml, and in which (C) provides a fixed negative charge;
- (2) a device containing (A);
- (3) a method for preparing (A);
- (4) a method for separating positively charged molecules (D) from a fluid by retaining them on (A); and
- (5) a process for transferring biomolecules (E) from an electrophoretic gel by treating the gel with (A).

USE - (A) are especially used, as ion-exchange materials, for removal (purification) of positively charged biomolecules (especially proteins, polypeptides, amino acids and nucleic acids) from solution, specifically for transferring them from an electrophoretic gel. Other applications are purification of human **albumin** from serum; in therapeutic fractionation of blood; separation of components from genetically engineered cell cultures or fermentation broths, and purification of viral vaccines and viral gene therapy vectors.

ADVANTAGE - (A) have high charge density; water-flow rates (e.g. 25-100 ml/min/square cm under 24 inches of **mercury**) and dynamic binding capacity (25-120 mg lysozyme/ml) but low non-specific protein binding. Proteins do not leach, before breakthrough; the membranes are practically free from grafts or covalent links to the substrate, and they can be prepared relatively simply. Where (A) includes a hydrophilic monomer, the distance between anionic groups is increased, reducing inter- and intra-chain associations, making the negative charges more readily available for interaction with positively charged substances.

DESCRIPTION OF DRAWING(S) - The figure depicts the breakthrough curve for lysozyme obtained from a membrane as described in the patent.  
Dwg.0/3

L27 ANSWER 4 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
AN 2000-442393 [38] WPIDS  
DNN N2000-330083 DNC C2000-134555  
TI Reagents for assaying conjugated bilirubin contain chelating agent, metal ion and/or metal complex to inhibit reactivity with unconjugated bilirubin and **albumin**-bonded bilirubin.  
DC B04 D16 J04 S03  
IN MORIMOTO, Y  
PA (NNTR) NIPPON SHOJI KK; (AZWE-N) AZWELL INC  
CYC 20  
PI WO 2000036140 A1 20000622 (200038)\* JA 28p  
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE  
W: US  
JP 2000166595 A 20000620 (200040) 10p  
ADT WO 2000036140 A1 WO 1999-JP6820 19991206; JP 2000166595 A JP 1998-352611 19981211  
PRAI JP 1998-352611 19981211  
AB WO 200036140 A UPAB: 20000811  
NOVELTY - Reagents for assaying conjugated bilirubin comprise agents for assaying bilirubin, and a chelating agent, metal ion and/or metal complex as reagents which selectively inhibit reactivity with unconjugated bilirubin and/or **albumin**-bonded bilirubin, are new.  
USE - The reagents are useful for assaying conjugated bilirubin especially in the presence of unconjugated bilirubin and/or **albumin**-bonded bilirubin e.g. for detecting or monitoring hepatic disorders, diseases and function.  
ADVANTAGE - The assay is selective for bilirubin as the reagents inhibit the reactivity of unconjugated bilirubin and/or **albumin**-bonded bilirubin.  
Dwg.0/0

L27 ANSWER 5 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
AN 2000-293112 [25] WPIDS  
DNC C2000-088635  
TI Mutant human beta-globin polypeptides used for generating a blood substitute to supplement the oxygen-carrying capacity of a patient's blood comprises substitution or deletion of native cysteine residues.  
DC B04 D16  
IN FRONTICELLI, C

PA (UTEM) UNIV TEMPLE

CYC 90

PI WO 2000018802 A1 20000406 (200025)\* EN 42p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES  
FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS  
LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ  
TM TR TT UA UG US UZ VN YU ZA ZW

AU 9965041 A 20000417 (200035)

EP 1117690 A1 20010725 (200143) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
RO SE SI

ADT WO 2000018802 A1 WO 1999-US22756 19990930; AU 9965041 A AU 1999-65041  
19990930; EP 1117690 A1 EP 1999-953002 19990930, WO 1999-US22756 19990930

FDT AU 9965041 A Based on WO 200018802; EP 1117690 A1 Based on WO 200018802

PRAI US 1998-102640P 19981001

AB WO 200018802 A UPAB: 20000524

NOVELTY - A human beta -globin mutant polypeptide (I) comprising the amino acid sequence of normal human beta -globin modified by the substitution or deletion of Cys residues at positions 93 and 112 and the substitution of a Cys for a non-Cys residue at one other position in the polypeptide, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a nucleic acid sequence (II) encoding a mutant beta -globin polypeptide (III) which has a defined sequence of 146 amino acids given in the specification;

(2) a vector comprising a promoter operably linked to (II) capable of directing the expression of a mutant beta -globin polypeptide;

(3) a host cell transformed with the vector of (2);

(4) a method for producing a human beta -globin mutant polypeptide comprising growing a culture of transformed host cells of (3) under conditions conducive to the expression of the polypeptide by the host cells;

(5) a modified human hemoglobin (IV) comprising (I) or (III);

(6) a polymeric hemoglobin (V) comprising (IV) where adjacent hemoglobins are covalently bonded to each other by one or more disulfide bridges formed by cysteine amino acid residues;

(7) a blood substitute comprising (V);

(8) a method of supplementing the oxygen-carrying capacity of a patient's blood comprising administering the blood substitute of (7); and

(9) a mutant human alpha -globin polypeptide (VI) comprising the amino acid sequence of normal human alpha -globin modified by the substitution or deletion of Cys at position 104.

ACTIVITY - Antianemic.

No biological data.

MECHANISM OF ACTION - Oxygen-carrier.

USE - The mutant alpha and beta -globin polypeptide sequences can be used to generate a modified human hemoglobin which is used to prepare a blood substitute for supplementing the oxygen-carrying capacity of a patient's blood (claimed). The blood substitute may be administered to any patient in a situation requiring supplementation of the oxygen-carrying capacity of the patient's blood.

ADVANTAGE - The mutant hemoglobin provided has high oxygen carrying capacity but low oncotic pressure which makes it useful as a blood substitute. A stable preparation of homogenous polymers is provided with the same characteristics unlike heterogeneous polymers of the prior art whose properties are difficult to control.

Dwg.0/3

L27 ANSWER 6 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
AN 2000-194945 [17] WPIDS  
DNC C2000-060366  
TI Polymer carriers for keratinocyte cultivation to cover skin defects e.g. burns, trophic ulcers and bedsores, avoid presence of feeder cells from cultivation system loading immunological system.  
DC A12 A14 A96 B04 D16  
IN DVORANKOVA, B; LABSKY, J; SMETANA, K; VACIK, J  
PA (UYKA-N) UNIV KARLOVA; (UYKA-N) UNIV KARLOVY 1 LEKARSKA FAKULTA; (UYKA-N) UNIV KARLOVY 3 LEKARSKA FAKULTA; (MAKR-N) USTAV MAKROMOLEKULARNI CHEM AVCR  
CYC 82  
PI WO 9964563 A1 19991216 (200017)\* EN 30p  
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
OA PT SD SE SL SZ UG ZW  
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU DE DK EE ES FI GB GE GH  
GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK  
MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US  
UZ VN YU ZW  
AU 9940293 A 19991230 (200022)  
CZ 9901946 A3 20010117 (200107)  
CZ 9901947 A3 20010117 (200107)  
ADT WO 9964563 A1 WO 1999-CZ17 19990609; AU 9940293 A AU 1999-40293 19990609;  
CZ 9901946 A3 CZ 1999-1946 19990602; CZ 9901947 A3 CZ 1999-1947 19990602  
FDT AU 9940293 A Based on WO 9964563  
PRAI CZ 1999-1947 19990602; CZ 1998-1803 19980610; CZ 1999-1946 19990602  
AB WO 9964563 A UPAB: 20000405  
NOVELTY - Polymer carriers for keratinocyte cultivation prepared by radical polymerization of polymerization mixture containing (weight%): polymerizable monomers (1-95), crosslinker (0-10), initiator (0-10), solvent (0-60), polymerizable saccharide or disaccharide derivatives (0-60), polymerizable sterically hindered amine derivatives (0-50), polymerizable alpha-amino acid derivatives (0-30) or their reactive derivatives.  
ACTIVITY - Wound healing; burn healing; ulcer healing; bed sore healing.  
USE - Used for cultivation of keratinocytes (claimed) to cover large skin defects such as burns, trophic ulcers and bedsores. Three standard polymer carriers and ten test polymer carriers were tested for adhesion of human keratinocytes after preincubation with bovine serum in presence of mouse fibroblasts or after adsorption of bioactive saccharides in absence of mouse fibroblasts. Adhesion of four test compounds was better compared with the three standards, although activation of the base using sugars was necessary. Four test carriers showed very good keratinocyte cultivation, with keratinocytes adhering and growing without prior pre-incubation with bioactive polysaccharides.  
ADVANTAGE - Avoids presence of feeder cells from cultivation system loading patient's immunological system. Does not possess properties that suppress formation of **free radicals** or reactive oxygen products to healing of affected tissues difficult. Allows application of autologous and allogenic cells to stimulate healing. Immunological loading of patient is lower and process of keratinocyte transplantation is simpler and more effective.  
Dwg.0/0

L27 ANSWER 7 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
AN 1999-580278 [49] WPIDS  
DNC C1999-168770  
TI Crosslinkable macromer systems for use in the preparation of matrices.

DC A11 A12 A14 A18 A35 A60 A96 B07 D22 E19

IN ANDERSON, A B; CHUDZIK, S J

PA (SURM-N) SURMODICS INC

CYC 23

PI WO 9947129 A1 19990923 (199949)\* EN 41p

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: AU CA JP MX

US 6007833 A 19991228 (200007)

AU 9929035 A 19991011 (200008)

US 6156345 A 20001205 (200066)

EP 1063975 A1 20010103 (200102) EN

R: DE ES FR GB IE IT

ADT WO 9947129 A1 WO 1999-US5244 19990311; US 6007833 A Provisional US 1998-78607P 19980319, US 1998-121248 19980723; AU 9929035 A AU 1999-29035 19990311; US 6156345 A Provisional US 1998-78607P 19980319, Div ex US 1998-121248 19980723, US 1999-469976 19991221; EP 1063975 A1 EP 1999-909954 19990311, WO 1999-US5244 19990311

FDT AU 9929035 A Based on WO 9947129; US 6156345 A Div ex US 6007833; EP 1063975 A1 Based on WO 9947129

PRAI US 1998-121248 19980723; US 1998-78607P 19980319; US 1999-469976 19991221

AB WO 9947129 A UPAB: 19991124

NOVELTY - Crosslinkable macromer system comprising one or more polymers providing pendent polymerizable and pendent initiator groups and where the system is adapted for polymerization to form a matrix for in vivo application, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a method of forming a polymeric matrix adapted for in vivo application, comprising applying the aforementioned macromer system to a substrate and cross-linking the system by **free radical** polymerization;

(2) a polymeric matrix adapted for in vivo application, consisting of the aforementioned macromer system which has been crosslinked by **free radical** polymerization.

USE - The matrix is used for cell immobilization, in the preparation of tissue adhesives and sealants, in controlled drug delivery, as well as in situ device formation (e.g. in the preparation of three-dimensional bodies for implants). Polymeric matrices can also be used in wound dressing, tissue replacement/scaffolding, cellular encapsulation.

ADVANTAGE - The macromer system has advantages over the use of polymerizable macromers and separate, low molecular weight initiators e.g. optimal combination of non-toxicity, efficiency and solubility. A collagen scaffolding containing a bone morphogenic protein was prepared from a solution of liquid macromer consisting of polymerizable collagen (5 w/v%) plus photoderivatized polyacrylamide in phosphate buffered saline (pH 7.4) which was treated with bone morphogenic protein (BMP-7) (50  $\mu$ g/ml, 0.005 w/v%). Aliquots (150  $\mu$ l) of the above solution were placed in molds (8 mm diameter, 3 mm high) and were illuminated for 10 seconds with a Dymax lamp to solidify the collagen scaffolding. Control disks of solidified scaffolding were prepared via the same protocol, except that BMP-7 was not added. The scaffolding was evaluated for stimulation of bone growth in a rat cranial onlay implant model. When evaluated histologically, the scaffolding containing BMP-7 showed extensive bone formation in the space originally occupied by the collagen disk. The amount of bone that formed with the controls was less than 25% of that observed with the BMP-7-containing disks, thus demonstrating that the solidified collagen scaffolding greatly enhanced BMP-stimulated bone formation.

Dwg.0/0

L27 ANSWER 8 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1999-243660 [20] WPIDS  
 DNC C1999-071030  
 TI Preventing or treating cell, tissue, organ or animal for reperfusion injury.  
 DC B03 B05 D16 D22  
 IN DODD-O, J M; PEARSE, D B  
 PA (UYJO) UNIV JOHNS HOPKINS SCHOOL MEDICINE  
 CYC 82  
 PI WO 9912539 A1 19990318 (199920)\* EN 36p  
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
 OA PT SD SE SZ UG ZW  
 W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE  
 GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG  
 MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG  
 UZ VN YU ZW  
 AU 9892261 A 19990329 (199932)  
 US 6090851 A 20000718 (200037)  
 ADT WO 9912539 A1 WO 1998-US18735 19980909; AU 9892261 A AU 1998-92261  
 19980909; US 6090851 A Provisional US 1997-58446P 19970910, Provisional US  
 1998-71188P 19980112, US 1998-150069 19980909  
 FDT AU 9892261 A Based on WO 9912539  
 PRAI US 1998-71188P 19980112; US 1997-58446P 19970910; US 1998-150069  
 19980909  
 AB WO 9912539 A UPAB: 19990525  
 NOVELTY - Preventing or treating a cell, tissue, organ or animal for  
 reperfusion injury comprises administration of a reduced form of  
 nicotinamide adenine dinucleotide phosphate (NADPH) oxidase inhibitor to  
 the cells, tissues, organs or animals.  
 MECHANISM OF ACTION - NADPH-oxidase inhibitor.  
 17 Sheep lungs were subjected to 30 minutes of ischaemia and 180  
 minutes of reperfusion with autologous blood. Diluent or 3 mM, 0.3 mM or  
 0.03 mM apocynin was administered to the pulmonary artery early in  
 ischemia and the reservoir before perfusion. After reperfusion, the lungs  
 were excised and subjected to increased static vascular pressures to  
 measure the reflection coefficient for **albumin**, the filtration  
 coefficient and extravascular lung water.  
 Results showed that 3 mM apocynin completely prevented decrease in  
 reflection coefficient of **albumin** and the increase in  
 extravascular lung water caused by ischemia, which showed that NADPH  
 oxidase contributed to reperfusion injury in sheep lungs.  
 USE - Used to treat or prevent reperfusion injury associated with  
 surgical procedures, especially cardiac surgery involving cardiopulmonary  
 bypass, or transplantation of cells, tissue or an organ including lungs,  
 heart, liver, intestine, pancreas, kidney, brain or limb (claimed). The  
 method may be used to treat reperfusion injuries to a cell, whether in  
 vitro for transplantation or research or in vivo including reperfusion  
 injuries due to ischemia or hypoxia. The reperfusion injury treated may be  
 due to direct exposure of a cell, tissue, organ or organism to reperfusion  
 injury-inducing symptoms e.g. ischemia or hypoxia and/or indirect exposure  
 such as exposure to another cell, tissue or organ exposed to reperfusion  
 injury-inducing conditions e.g. ischemia or hypoxia. The injury may be  
 associated with reperfusion-stimulated neutrophil activation such as that  
 associated with a surgical procedure, e.g. cardiopulmonary bypass that  
 involves pulmonary, cardiac and vascular dysfunction, cell/tissue/organ  
 transplantation, such as orthotopic lung transplant, pulmonary embolus,  
 thoracic surgery involving prolonged compression of the lung, stroke,  
 trauma, seizure, myocardial infarction, angioplasty, ischemic bowel  
 syndrome, ulcers, skin and muscle flaps (e.g. generated during injury or  
 surgery), hypothermia (e.g. frostbite), reattachment of a body part and

neutrophil activation-associated damage of the lung, liver and kidney associated with distal ischemia reperfusion injury.

ADVANTAGE - In contrast to prior-art neutrophil-depleting agents, (I) are safe when given systemically for weeks or months. In contrast to prior-art **free-radical** scavenging agents, (I) do not result in production of potentially dangerous compounds such as hydrogen peroxide. In contrast to prior-art agents that increase intracellular cyclic AMP, (I) completely block reperfusion injury to the lung without activating ubiquitous signal transduction system that may lead to side-effects.

Dwg.0/0

L27 ANSWER 9 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1998-335297 [30] WPIDS  
 DNC C1998-103984  
 TI New organo-selenium and seleno-sulphide antioxidant agents - inhibit TNF induced interleukin release, use to preserve organs for transplants, inflammation, e.g., bowel, ARDS, glaucoma and AIDS.  
 DC B05  
 IN CHAUDIERE, J; ERDELMEIER, I; MOUTET, M; TAILHAN-LOMONT, C; YADAN, J; CHAUDIERE, J R; TAILHAN, L C; YADAN, J C  
 PA (OXIS-N) OXIS ISLE OF MAN LTD; (OXIS-N) OXIS INT SA  
 CYC 28  
 PI EP 850924 A1 19980701 (199830)\* EN 48p  
 R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI  
 FR 2757857 A1 19980703 (199833)  
 AU 9852740 A 19980702 (199837)  
 CA 2225903 A 19980627 (199841)  
 JP 10330355 A 19981215 (199909) 26p  
 US 5973009 A 19991026 (199952)  
 US 6040328 A 20000321 (200021)  
 EP 850924 B1 20010314 (200116) EN  
 R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE  
 DE 69704255 E 20010419 (200129)  
 AU 736842 B 20010802 (200152)  
 ES 2157524 T3 20010816 (200156)  
 ADT EP 850924 A1 EP 1997-204070 19971223; FR 2757857 A1 FR 1996-16103 19961227; AU 9852740 A AU 1998-52740 19980127; CA 2225903 A CA 1997-2225903 19971224; JP 10330355 A JP 1998-561 19980105; US 5973009 A US 1997-997669 19971223; US 6040328 A Div ex US 1997-997669 19971223, US 1999-387593 19990831; EP 850924 B1 EP 1997-204070 19971223; DE 69704255 E DE 1997-604255 19971223, EP 1997-204070 19971223; AU 736842 B AU 1998-52740 19980127; ES 2157524 T3 EP 1997-204070 19971223  
 FDT US 6040328 A Div ex US 5973009; DE 69704255 E Based on EP 850924; AU 736842 B Previous Publ. AU 9852740; ES 2157524 T3 Based on EP 850924  
 PRAI FR 1996-16103 19961227  
 AB EP 850924 A UPAB: 19980730  
 Organoselenium compounds of formula (I), and their salts are new: R = H or CR<sub>1</sub>R<sub>2</sub>-A-B; R<sub>1</sub>, R<sub>2</sub> = lower alkyl, aryl (optionally substituted) or lower aralkyl (optionally substituted); A = CO or (CR<sub>3</sub>R<sub>4</sub>)<sub>n</sub>; B = NR<sub>5</sub>R<sub>6</sub>, N+R<sub>5</sub>R<sub>6</sub>R<sub>7</sub> -, OR<sub>5</sub> or SR<sub>5</sub>; Ar = optionally substituted phenyl group or heterocyclyl, provided R = C(R<sub>1</sub>R<sub>2</sub>)-A-B; or Ar = a different heterocyclyl, provided R = H; Z = O, S or NR<sub>5</sub>; X = Ar(R)-Se, -S-glutathione, -S-N-acetylcysteine, -S-cysteine, -S-penicillamine, -S-albumin, -S-glucose or one of eight amide containing groups; R<sub>3</sub>, R<sub>4</sub> = H, lower alkyl, aryl (optionally substituted) or lower aralkyl (optionally substituted); R<sub>5</sub> = R<sub>3</sub>, heteroaryl (optionally substituted), lower heteroaralkyl (optionally substituted), lower alkylcarbonyl, arylcarbonyl, lower alkylsulphonyl or arylsulphonyl; R<sub>6</sub>, R<sub>7</sub> = R<sub>3</sub>, heteroaryl (optionally

substituted) or lower heteroaralkyl (optionally substituted);  $n = 0-1$ ;  $X^+ =$  cation; and  $Y^- =$  anion; provided that when: (a)  $R = CR_1R_2CR_3R_4-B$  (where  $B = NR_5R_6$  or  $N+NR_5R_6R_7 Y^-$ ); and  $X = Ar(R)-Se-$  (where  $Ar =$  phenyl (optionally substituted)) then  $CR_1R_2$  is different from  $CR_3R_4$ ; and (b)  $Ar =$  phenyl;  $R = CR_1R_2-CO-B$  (where  $B = NH_2, NHCH_3, NHCH_2Ph$  or  $NHPh$ ); and  $X = Ar(R)-Se-$  then  $R_1$  and  $R_2$  are not both  $CH_3$ .

USE - (I) are useful as antioxidants, particularly for preserving media of grafts for transplantation of organs, e.g. hearts, livers, kidneys and lungs. (I) are used in antioxidant compositions useful for the treatment of: (a) physiopathological conditions in which an over production of cytotoxic hydroperoxides contribute to impairments of cells or tissues; (b) inflammatory and/or ischaemic cardio- and cerebrovascular pathologies, e.g. arterial restenoses following angioplasty, arterial stenoses following artery allografts, treating intermittent claudication of obstructive ischaemia and treatments of cerebrovascular accidents of ischaemic origin; (c) inflammatory and/or ischaemic digestive pathologies, e.g. acute inflammation of the bowel (Crohn's disease and haemorrhagic rectocolitis); (d) inflammatory and/or ischaemic respiratory pathologies e.g. adult respiratory distress syndrome (ARDS) and infant respiratory distress syndrome (IRDS); (e) glaucoma; (f) cataracts; (g) acute ophthalmic allergies; (i) impairments of the retina associated with macular degeneration; (j) viral infections causing immuno-deficiency e.g. acquired immuno deficiency distress syndrome (AIDS); and (k) post-radiotherapy fibroses (all claimed). The composition is used for the treatment of any physiopathological condition in which an over-production of cytotoxic hydroperoxides contributes to the functional impairments of cells or tissues. This over-production of hydroperoxide can be due: (i) to the activation of the intra-cellular metabolic pathways such as those of the flavine or cytochrome P-450 oxygenases, lipoxygenases and monoamine oxidases; (ii) to the activation of enzymes contained in endothelial cells (xanthine oxidase, 15-lipoxygenase) or in blood platelets (cyclooxygenase and 12-lipoxygenase); (iii) to the activation, by cytokines such as TNF-A, of inflammatory and/or immune cells such as neutrophils, macrophages or lymphocytes; (iv) to an intoxication by a **free-radical** generating xenobiotic; or (v) to a voluntary irradiation, such as practised during a radiotherapy, or an accidental irradiation (all claimed).

ADVANTAGE - Preparations of these compounds by the present route are easy to carry out and give good yields. In particular, very few 4(5)-selenoimidazoles have been prepared in the literature, either by use of silyl protections, or from 4-halo-imidazoles and selenourea or  $NaSeH$ .  
Dwg.0/3

L27 ANSWER 10 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
AN 1994-007206 [01] WPIDS  
DNC C1994-002820  
TI Modified arabino galactan as carrier for therapeutic agents e.g. antivirals or anti sense DNA - provides targetted delivery to cells with the asialo glyco protein receptor, esp. hepatocyte(s).  
DC A96 B04 B07 D16  
IN ENRIQUEZ, P; JOSEPHSON, L; JUNG, C; PALMACCI, S; ENRIQUES, P  
PA (ADMA-N) ADVANCED MAGNETICS INC  
CYC 18  
PI WO 9325239 A1 19931223 (199401)\* EN 35p  
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE  
W: CA JP NO  
NO 9404838 A 19950217 (199516)  
EP 646018 A1 19950405 (199518) EN  
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE  
JP 07507794 W 19950831 (199543) 10p



ADT WO 9325239 A1 WO 1992-US5091 19920617; NO 9404838 A WO 1992-US5091 19920617, NO 1994-4838 19941214; EP 646018 A1 EP 1992-914217 19920617, WO 1992-US5091 19920617; JP 07507794 W WO 1992-US5091 19920617, JP 1994-501422 19920617

FDT EP 646018 A1 Based on WO 9325239; JP 07507794 W Based on WO 9325239

PRAI EP 1992-914217 19920617; WO 1992-US5091 19920617; NO 1994-4838 19941214

AB WO 9325239 A UPAB: 19940217

Carrier which forms a complex with a therapeutic agent (I) for delivery to a cell receptor on the surface of target tissue comprises arabinogalactan (AG) modified by a functional residue to produce a deriv. which retains affinity for the receptor.

Pref. AG is modified at one or more OH sites; the functional gp. introduced is phosphoryl, SH, NH<sub>2</sub>, halo, acylimidazole or COOH, or the functional residue is a polymer, pref. dextran, dextrin, albumin or poly-L-lysine.

Pref. antiviral agents are acyclovir; adenine arabinoside-5'-monophosphate (Ara-AMP), or Ara-A; the protective agent is S-2-(3-aminopropylamino)-ethylthiophosphoric acid; scavengers are e.g. melanin, cysteamine derivs. or Vitamin E derivs.

USE/ADVANTAGE - The complexes are used to deliver, as (I), antivirals; radio- or chemo-protective agents, **free radical** scavengers; polypeptides, antibodies or their fragments (directed e.g. against hepatitis B virus); DNA (partic. antisense) or antiinflammatory steroids. They are targetted to cells carrying the asialoglycoprotein receptor, esp. hepatocytes, and precise targetting should reduce side effects of (I).

Unlike glycoproteins previously suggested as carriers, AG is unlikely to be contaminated by human viruses; can tolerate contact with organic solvent; has only a limited variety of reactive sites; has low toxicity and antigenicity, and has natural affinity for the specified receptor (eliminating need for a deasialylation reaction).

Dwg. 0/0

L27 ANSWER 11 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1989-235761 [33] WPIDS

DNC C1989-104985

TI New covalent conjugate of 3-bonded vinca alkaloid - with protein carrier useful as anticancer agents with controlled targetting and reduced toxicity.

DC B02

IN BHUSHANA, R; COLLARD, M P; DEJONGHE, J P; TROUET, A; COLLARD, M; DEJONGHE, J

PA (IREC-N) IRE CELLTARG SA; (WALL-N) LA REGION WALLONNE; (IREC-N) IRE-CELLTARG SA

CYC 16

PI EP 328446 A 19890816 (198933)\* FR 16p  
 R: AT BE CH DE ES FR GB GR IT LI LU NL SE  
 FR 2626882 A 19890811 (198939)  
 JP 02152992 A 19900612 (199029)  
 US 5024835 A 19910618 (199127) 11p  
 EP 328446 B1 19940720 (199428) FR 28p  
 R: AT BE CH DE ES FR GB GR IT LI LU NL SE  
 DE 68916820 E 19940825 (199433)  
 ES 2057157 T3 19941016 (199442)  
 CA 1336119 C 19950627 (199533) FR  
 JP 2930965 B2 19990809 (199937) 13p

ADT EP 328446 A EP 1989-400334 19890207; US 5024835 A US 1989-306639 19890203;  
 EP 328446 B1 EP 1989-400334 19890207; DE 68916820 E DE 1989-616820  
 19890207, EP 1989-400334 19890207; ES 2057157 T3 EP 1989-400334 19890207;

CA 1336119 C CA 1989-590274 19890207; JP 2930965 B2 JP 1989-27744 19890208  
 FDT DE 68916820 E Based on EP 328446; ES 2057157 T3 Based on EP 328446; JP  
 2930965 B2 Previous Publ. JP 02152992  
 PRAI FR 1988-1439 19880208  
 AB EP 328446 A UPAB: 19930923

New conjugate (I) comprises a vinca (indole-dihydroindole) deriv. having on C3 a 'detergent' chain of at least 7 aliphatic C bonded covalently to a natural polypeptide (II) as macromolecular carrier.

Pref. the chain has a terminal COOH for coupling, as peptide, to a free amino gp. in (II). Pref. (I) are of formula (7a) (R1,R2) = (Et,OH) or (H,Et) R4 = H, Me or CHO; R3 = OH or OCOMe; R = -A-R'-CO-; A = NH, NH-alk-COO, NH-alk-CONH-, or is the divalent residue of an amino acid present in proteins and endig in NH and COO or NH and CONH alk = opt. branched 1-7C aliphatic hydrocarbon chain; R' = gp. w/lt at least 7 aliphatic C; R is substd. by CO (from terminal COOH) and is coupled to free amino in T via CONH; T = residue of (II); -RT can also be -A-R'-CONH-P, with NHP = T.

USE/ADVANTAGE - (I) are useful as anticancer agents having (compared with the free alkaloids) better selectivity and activity, and lower inherent toxicity. Component (II) provides targetted delivery to the cancer cells; e.g., where (II) is galactosylated human **albumin** (GHA) the conjugate is specific for hepatocytes and human hepatoma cells.  
 0/3

L27 ANSWER 12 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1988-279549 [40] WPIDS

DNN N1988-212193 DNC C1988-124441

TI Low mol. wt. mimic of superoxidedismutase - comprises water-soluble complex formed between chelating agent and **manganese**, used for treating inflammation, etc..

DC B05 C03 P34

IN DARR, D J; FRIDOVICH, I

PA (UYDU-N) UNIV DUKE

CYC 15

PI EP 284645 A 19881005 (198840)\* EN 12p  
 R: AT BE CH DE ES FR GB GR IT LI LU NL SE

JP 63250392 A 19881018 (198847)

US 5223538 A 19930629 (199327) 6p

ADT EP 284645 A EP 1987-106684 19870508; JP 63250392 A JP 1987-120335  
 19870519; US 5223538 A US 1987-32475 19870331

PRAI US 1987-32475 19870331

AB EP 284645 A UPAB: 19930923

A low mol. wt. mimic of superoxide dismutase is claimed comprising a water-soluble complex formed between a chelating agent and **manganese**, the complex being capable of catalysing the dismutation of superoxide radicals and capable of retaining its activity in the presence of proteins.

Suitable chelating agents are siderophores, pref. of the hydroxamate type, esp. desferrioxamine or an analogue or deriv.

USE - The mimic catalyses the dismutation of O2(-) and retains its activity in the presence of serum **albumin** and cellular extracts contg. protein. It is useful for treating inflammation, extending the storage lifetime of organs and tissues intended for transplantation, decreasing damage to the heart suffered as a consequence of infarction, protecting against tissue death and necrosis following any situation entailing temporary cessation of circulation to a tissue or organ, as a radioprotectant and as an antioxidant applicable to any **free radical** chain oxidation in which O2(-) serves either as initiator or chain propagator. It may also be useful in inhibiting autoxidation reactions, thus providing increased shelf life for e.g. food prod.,

pharmaceuticals and stored blood. It may also be used for protecting plant cells from the toxicity of superoxide radicals.  
0/2

L27 ANSWER 13 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1986-126270 [20] WPIDS  
 CR 1984-213350 [34]; 1986-056863 [09]; 1986-056864 [09]; 1989-007515 [01];  
 1991-021596 [03]; 1991-332540 [45]; 1996-208134 [20]  
 DNC C1986-053835  
 TI High purity immunoglobulin G prodn. from animal plasma - by  
 filtration-adsorption and ion exchange chromatography esp. when  
 transferrin and **albumin** are also isolated.  
 DC A96 B04  
 IN COGSWELL, G  
 PA (AMMA) AMF INC; (CUNO-N) CUNO INC; (HOUK-I) HOU K C; (HOUK-I) HOU K C  
 CYC 13  
 PI EP 180766 A 19860514 (198620)\* EN 154p  
 R: AT BE CH DE FR GB IT LI LU NL SE  
 JP 61087631 A 19860506 (198624)  
 US 4639513 A 19870127 (198706)  
 ADT EP 180766 A EP 1985-112468 19851002; JP 61087631 A JP 1985-216307  
 19851001; US 4639513 A CIP of US 1983-466114 19830214, CIP of US  
 1984-576448 19840202, CIP of US 1984-643212 19840822, CIP of US  
 1984-643613 19840822, US 1984-656922 19841002  
 PRAI US 1984-656922 19841002; US 1983-466114 19830214; US 1984-576448  
 19840202; US 1984-643212 19840822; US 1984-643613 19840822  
 AB EP 180766 A UPAB: 19960604  
 (1) Prodn. of high purity immunoglobulin G (IgG) from animal plasma  
 comprises (a) diluting the plasma; (b) sepng. sparingly soluble and  
 insoluble plasma components by filtration/adsorption, so that the  
 adsorbability of proteolytic enzymes is potentiated, to give extraneous  
 protein-contg. IgG; and (c) sepng. the IgG from the protein-contg. IgG by  
 ion-exchange chromatography, opt. followed by affinity chromatography.  
 (2) Continuous prodn. of IgG, transferrin (I) and **albumin** (II)  
 from animal plasma comprises (a) diluting the plasma; (b) filtering/  
 adsorbing the plasma to separate sparingly soluble and pptd. plasma  
 components to give a first filtrate; (c) passing the filtrate through a  
 first ion-exchange column to give an adsorbed fraction and an unadsorbed  
 fraction. The adsorbed fraction contains (I) and (II) and some IgG, and  
 the unadsorbed fraction contains most of the IgG; (d) eluting the (I) and  
 part of the (II); (e) eluting the remaining (II); and (f) using a further  
 series of adsorptions on ion-exchange resins and elutions to give the  
 prods.  
 USE/ADVANTAGE - High purity IgG suitable for intravenous injection is  
 obtd. in high yields. The prod. is remarkably free from aggregates,  
 fragments, proteolytic enzymes, enzyme activators, coagulating factors  
 etc., and it has much reduced anticomplementary activity. Highly pure (I)  
 and (II) may also be obtd. The IgG is injected into humans to give high  
 levels of antibodies, so that they can combine specifically with antigens  
 such as viruses and bacteria.  
 0/0  
 Dwg. 0/0